FOOD AND DRUG ADMINISTRATION

CENTER FOR TOBACCO PRODUCTS (CTP)

TOBACCO PRODUCTS SCIENTIFIC ADVISORY COMMITTEE (TPSAC)

FRIDAY, JULY 16, 2010

8:00 a.m. to 3:30 p.m.

Gaithersburg Marriott Washingtonian Center

9751 Washingtonian Boulevard

Rockville, Maryland

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I N D E X

P R O C E E D I N G S

(8:30 a.m.)

DR. SAMET: Good morning. I'll take the hushed silence again as a signal that it's time to get going. I'm John Samet, the chair of the Tobacco Products Scientific Advisory Committee. Good morning to all.

As a new Californian, I'm pleased to be here during the biggest earthquake to strike. I understand that there are reports on the news of crooked pictures on walls.

[Laughter.]

DR. SAMET: On to more serious matters. For topics such as those being discussed at today's meeting, there are often a variety of opinions, some of which are quite strongly held. Our goal is that today's meeting will be a fair and open forum for discussion of these issues and that individuals can express their views without interruption.

Thus, as a gentle reminder, individuals will be allowed to speak into the record only if recognized by the chair. We look forward to a productive meeting.

In the spirit of the Federal Advisory Committee Act and the Government in the Sunshine Act, we ask that the advisory committee members take care that their conversations about the topic at hand take place in the open forum of the

meeting.

We are aware that members of the media are anxious to speak with the FDA about these proceedings. However, FDA will refrain from discussing the details of this meeting with the media until its conclusion.

Also, the committee is reminded to please refrain from discussing the meeting topic during breaks or lunch. Thank you.

We do have an open public hearing scheduled at 10:10. We have a number of scheduled presenters. There is a signup sheet for those who wish to make presentations during the session.

I will note that the time is quite limited and we will see how many presenters have signed up. It's likely that your allotted time to speak will be, at the most, three minutes. So we will watch the number of people who are interested in signing up and decide if we can accommodate you during that session. The signup sheet is outside.

So let's begin with committee introductions. I'll start again with you, Dan.

DR. HECK: I am Dan Heck, a principal scientist at the Lorillard Tobacco Company, and I'm here representing the interests of the tobacco manufacturers.

DR. LAUTERBACH: Good morning. John Lauterbach, owner, Lauterbach & Associations, consultants in tobacco chemistry and toxicology, and I'm here representing the interests of the small business tobacco manufacturers.

MR. HAMM: Good morning. I'm Arnold Hamm, and I'm representing the interests of U.S. tobacco growers.

DR. KAROL: Good morning. I'm Susan Karol, the chief medical officer for the Indian Health Service.

DR. BAUER: Good morning. I'm Ursula Bauer, director of the National Center for Chronic Disease Prevention and Health Promotion at the Centers for Disease Control and Prevention.

DR. BACKINGER: Cathy Backinger, the chief of the Tobacco Control Research Branch at the National Cancer Institute, representing the

National Institutes of Health.

DR. CLANTON: I'm Mark Clanton, chief medical officer of the High Plains Division of the American Cancer Society, and I'm here as a pediatrician, public health expert, and my experience in oncology.

MS. DELEEUW: Good morning. I'm Karen DeLeeuw, and I'm with the Colorado Department of Public Health and Environment, and the government representative.

MS. STARK: Good morning. I'm Christi Stark, the acting designated federal official.

DR. BENOWITZ: Neal Benowitz, Professor of Medicine, University of California-San Francisco.

DR. WAKEFIELD: Good morning. I'm Melanie Wakefield, director of the Center for Behavioral Research and Cancer at the Cancer Council Victoria, in Australia.

DR. HATSUKAMI: Good morning. I'm Dorothy Hatsukami from the University of Minnesota, Professor of Psychiatry.

DR. HENNINGFIELD: Good morning. I'm Jack Henningfield, Research and Health Policy at Pinney Associates, and Professor of Behavioral Biology at the Johns Hopkins University School of Medicine, and my expertise is primarily addiction.

DR. NEZ HENDERSON: Patricia Nez Henderson, Black Hills Center for American Indian Health.

DR. CONNOLLY: Good morning. My name is Greg Connolly, and I'm a professor at the Harvard School of Public Health.

DR. HUSTEN: I'm Corinne Husten, senior medical advisor at the Center for Tobacco Products, FDA.

DR. ASHLEY: I'm David Ashley. I'm director of the Office of Science, Center for Tobacco Products at FDA.

DR. DEYTON: Good morning. I'm Lawrence Deyton, director of the Center for Tobacco Products at FDA.

MS. STARK: At this time, I'm going to go ahead and read the meeting statement.

The Food and Drug Administration, FDA, is convening today's meeting of the Tobacco Products Scientific Advisory Committee under the authority of the Federal Advisory Committee Act, FACA, of 1972. With the exception of the industry representatives, all members and temporary nonvoting members are special government employees, SGEs, or regular federal employees from other agencies and are subject to federal conflict of interest laws and regulations.

The following information on the status of this committee's compliance with the federal ethics and conflict of interest laws covered by, but not limited to, those found at 18 USC Section 208 and Section 712 of the Federal Food, Drug, and Cosmetics Act, FD&C Act, is being provided to participants in today's meeting and to the public. FDA has determined that members of this committee are in compliance with federal ethics and conflict of interest laws.

Under 18 USC Section 208, Congress has authorized FDA to grant waivers to special

government employees and regular federal employees who have potential financial conflicts when it is determined that the agency's need for a particular individual's services outweighs his or her potential financial conflict of interest.

Under Section 712 of the FD&C Act, Congress has authorized FDA to grant waivers to special government employees and regular federal employees with potential financial conflicts when necessary to afford the committee essential expertise.

Related to the discussion of today's meeting, members of this committee have been screened for potential financial conflicts of interest of their own, as well as those imputed to them, including those of their spouses or minor children, and, for purposes of 18 USC Section 208, their employers.

These interests may include investments, consulting, expert witness testimony, contracts, grants, CRADAs, teaching, speaking, writing, patents and royalties, and primary employment.

Today's agenda involves, one, receiving updates on upcoming committee business related to menthol, including agency requests for information from industry on menthol cigarettes, in order to prepare for the Tobacco Products Scientific Advisory Committee's required report to the Secretary of Health and Human Services regarding the impact of use of menthol in cigarettes on the public health; and, two, receiving and discussing industry presentations on menthol in cigarettes as they relate to five topics: characterization of menthol; clinical effects of menthol; biomarkers of disease risk; marketing data; and, population effects.

These discussions are preliminary to the preparation of the Tobacco Products Scientific Advisory Committee's required report to the Secretary of Health and Human Services regarding the impact of use of menthol in cigarettes on the public's health.

This is a particular matters meeting during which general issues will be discussed.

Based on the agenda for today's meeting and all financial interests reported by the committee members, no conflict of interest waivers have been issued in connection with this meeting.

To ensure transparency, we encourage all committee members to disclose any public statements that they have made concerning the issues before the committee.

With respect to FDA's invited industry representatives, we would like to disclose that Drs. Daniel Heck and Lauterbach and Mr. Arnold Hamm are participating in this meeting as nonvoting industry representatives, acting on behalf of the interests of the tobacco manufacturing industry, the small business tobacco manufacturing industry, and tobacco growers, respectively. Their role at this meeting is to represent these industries in general and not any particular company.

Dr. Heck is employed by Lorillard Tobacco Company; Dr. Lauterbach is employed by Lauterbach and Associates, LLC; and, Mr. Hamm is retired.

FDA encourages all other participants to advise the committee of any financial relationships they may have with any firms at issue. Thank you.

At this point, I'd like to remind everyone present to please silence your cell phones, if you have not already done so.

I'd also like to identify the FDA press contact, Tesfa Alexander. If you're here present, please stand. Thank you.

DR. SAMET: Okay. I'm pleased to introduce Dr. Joshua Sharfstein, who was appointed by President Obama as FDA's Principal Deputy Commissioner in 2009. He served as acting Commissioner for Food and Drugs from March 29th through May 25th of 2009.

From December 2005 through March 2009, Dr. Sharfstein was the Commissioner of health for the City of Baltimore. And I will say that there we had the opportunity to work together in a partnership between the Bloomberg Public Health and the city.

Under his leadership, the Baltimore Health Department and its affiliated agencies won multiple national awards for innovative programs. In 2008, he was named a Public Official of the Year by GOVERNING Magazine.

Previously, Dr. Sharfstein served on the staff of the House Government Reform Committee and served as health policy adviser to Congressman Henry A. Waxman. Among the issues he worked on were HIV/AIDS, oversight of the FDA Tobacco and Public Health.

He's a native of Maryland and a 1991 graduate of Harvard College, a 1996 graduate of Harvard Medical School, 1999 graduate of the combined residency program in pediatrics at Boston Children's Hospital and Boston Medical Center, and a 2010 graduate of the fellowship in general pediatrics at the BU School of Medicine. Of course, he actually left Boston.

Thank you for joining us, Josh. We look forward to your remarks.

DR. SHARFSTEIN: Thank you very much.

I'm very pleased to be here. Thank you for the opportunity to talk with you. It's good to see you again, Dr. Samet. I think the last time we met may have been in east Baltimore.

I asked for this chance to come speak with you to express the appreciation of FDA for the remarkable commitment and expertise you've brought to the Scientific Advisory Committee.

As you heard, prior to FDA, I served as the City Health Commissioner of Baltimore. Before that, I served on the staff of Congressman Waxman, and I'm trained and have worked as a pediatrician. So as you can imagine, I had at least three good reasons to celebrate the passage of the Family Smoking Prevention and Tobacco Control Act last year.

This law is intended to improve health in the United States by protecting children from addiction and disease, helping tobacco users quit, and generally reducing the enormous toll of suffering and death from tobacco products in this country.

To succeed, FDA needs good advice. I want to take this opportunity to describe for you and the public how FDA assembled such a terrific group to help us as we launched tobacco regulation in the United States and how we address issues related to conflict of interest and bias.

I'm going to maybe give a little bit of the background to the statement that you just heard. Last fall, FDA received more than 100 nominations for the voting members of this committee. We then asked the Assistant Secretary for Health in the Department of Health and Human Services, Dr. Howard Coe, to bring together public health leaders from the National Institutes of Health, Centers for Disease Control and Prevention, and the Federal Trade Commission.

We gave this group the requirements of the Tobacco Control Act and a big pile of CVs. They then worked to identify top experts to advise our new program, experts like Dr. Samet, a member of the Institute of Medicine, who was twice awarded the Surgeon General's Medallion for his

work as editor for reports of the Surgeon General on tobacco; experts like Dr. Hatsukami, a professor of cancer prevention at the University of Minnesota, who edited the chapter on nicotine addiction in the Surgeon General's report on how tobacco causes disease; experts like Dr. Benowitz, the chief of clinical pharmacology at the UCSF School of Medicine, a past president of Society for Research on Nicotine and Tobacco, and one of the scientific editors of the NCI's monograph on the health risks of low tar cigarettes; experts like Dr. Melanie Wakefield, a leader in mass media, advertising, marketing, brand images and warning labels, and behavioral research; she served as a senior editor to the National Cancer Institute monograph on the role of media on promoting and reducing tobacco use; and, experts like Dr. Jack Henningfield, a global leader in addiction research, who has advised HHS, the World Health Organization, and the International Agency for Research on Cancer; he served as scientific editor of the report of the Surgeon General on the

health consequences of smoking and nicotine addiction.

I could go on and on and mention each one of you, but let me just say that we are honored to have such leading experts serve as advisors and we deeply appreciate your counsel and service.

Dr. Coe and his team did a terrific job identifying top experts, but that was just step one. We next evaluated conflict of interest before making analysis final selections. This is an obligation the agency takes very seriously for all of our external advisory committees, both in assembling the committee and before each and every meeting.

Our approach to the Tobacco Committee started with the fact that no voting member on this committee is permitted to have a financial interest in the tobacco industry during their service on the committee or for the 18 months prior to their appointment. This not only makes sense, it's specified in the law.

In addition, before each meeting, we

determine the agenda. We compile lists of products and firms that could be affected by the decision and outcomes of the meeting and any FDA decision based on the committee's recommendations. This list could include tobacco products, laboratory tests, even drugs and devices, if these will be discussed or implicated.

We send you this list, along with a confidential financial disclosure form and instructions for completing the form. Voting members then complete it, identifying all financial interests that they have in the products or firms. These financial interests, as you heard, include stocks and investments, consulting relationships, research support and grants, employment, patents, work as an expert witness, including the specific topics of expert witness testimony, and other activities.

We count imputed interests, such as grants to the institution and the interests of a spouse or minor child. This confidential information is then reviewed by staff from various

offices in accordance with FDA's procedures. These include the Center for Tobacco Products, FDA's advisory committee oversight and management staff, FDA's ethics and integrity staff, and, as necessary, the Office of General Counsel Ethics Division of the Department of Health and Human Services.

Based on these reviews, which are extensive, we consider whether the meeting will have a direct and predictable effect on these financial interests. If there is a disqualifying financial interest, we will generally ask that you recuse yourselves from the meeting. If there is such a conflict of interest, you do not participate, unless granted a waiver.

A waiver can only be granted under limited circumstances and would be made public. You would have heard the announcement. But we have not granted any waivers for TPSAC meetings for this committee to date.

According to our law and regulations, when specific products come under discussion, FDA

considers appearances that may arise from personal and business relationships in accord with the standards of ethical conduct for all government employees.

Again, with the guidance of ethics staff both at FDA and at the Department of Health and Human Services, we then determine whether an appearance concern outweighs the value of your contribution to a particular meeting.

When such issues arise, we may ask additional questions of you or ask you to step back from the meeting. In addition to taking steps to address conflict of interest, FDA regulations permit the agency to remove a member from an advisory committee who demonstrates bias that interferes with the ability to provide us with objective advice.

Now, in applying this rule, we understand that a stated opinion on a scientific matter does not necessarily mean that a member would have a closed mind on a particular issue. After all, by definition, experts have views about issues that

fall within their particular area of expertise.

I know that this whole process can be burdensome on you, but I also know why this process exists. It exists to ensure the integrity of the expert advice FDA receives on tobacco and all other issues handled by the agency. It is a process supported by the Department of Health and Human Services and recently affirmed by the Office of the Inspector General.

It is also a process, I want to be completely clear, that FDA stands behind. When questions are raised from any quarter, we review them. We take them seriously. We are prepared to take appropriate action when we find the concerns have merit, and we are prepared to hold steady when we find that the concerns are not justified.

Identifying top experts, applying our laws and regulations fairly, this is how we benefit from your expertise to develop an effective public health program on tobacco.

Again, thank you for your service. Good luck today.

DR. SAMET: Thank you, Dr. Sharfstein. We appreciate your comments. Thank you for coming.

We will move on to industry presentations. We're now with the panel on population effects.

Mr. Dillard, did you want to introduce the panel or should we just proceed?

MR. DILLARD: Proceed.

DR. SAMET: Thank you. Then we will proceed with the panel.

DR. CURTIN: I appreciate the opportunity to speak with you this morning on behalf of R.J. Reynolds Tobacco. My name is Jeff Curtin. I'm a principal scientist, and I currently serve as Director of Regulatory Science Development and Engagement.

We believe that it's imperative for the FDA, as a science-based organization, to be fully informed and accurately informed as to the existing and emergent science related to the topics under discussion; in this case, the

population level effects associated with menthol versus non-menthol cigarette use.

It would appear from the March meeting that the key issues under discussion are whether or not menthol cigarettes are preferentially used by adolescents compared to adults and whether menthol versus non-menthol cigarette use increases smoking initiation, smoking dependence, and reduces smoking cessation.

My task today will be to provide a comprehensive overview of the existing literature, what it does and does not indicate, and to provide recent findings from our own analysis of government survey data.

I was heartened to hear yesterday that the emerging whitepaper will include some of our comments to FDA on the existing literature. Having spent much time working on those comments, it was nice to know they would be considered. We have put those comments in two submissions. Much of the data I'll be discussing today on the population effects have not yet been published,

but we did provide them in the form of three draft manuscripts, I think, at the end of June.

So we've got quite a bit of data to go through, so let's get started. It is our intent to demonstrate that government survey data indicate no adverse population level effects associated with current menthol versus non-menthol cigarette use; specifically, no age-related differences, adolescents versus overall; an older age of smoking initiation for menthol versus non-menthol cigarette smokers; a lower average smoking intensity, indicating lower dependence for menthol versus non-menthol cigarette smokers; and, a higher percentage of adults attempting smoking cessation.

We would also contend that evidence-based conclusions require proper and consistent analysis of the population data and that these proper and consistent analyses are generally not provided by some of the available existing literature.

So first off, demographics of menthol cigarette use. And the way I'd like to structure

this talk, and I'll tell you now so it's easier to follow, is I'd like to review some of the conclusions from the first menthol meeting last March and then maybe augment those findings with our interpretation of the available literature, as well as some other publicly available data, and then I'll move into our findings from the four national surveys.

So during the initial meeting, it was concluded that menthol cigarette use is higher among adolescents, based on the data of a single survey; that is, the NSDUH. The data were from 2004 to 2008. This survey was suggested to be the only national survey that could effectively do this type analysis.

We would argue that the NHANES provides for analysis of menthol cigarette use among adolescents and adults and has the advantage of defining cigarette use based on usual brand versus a much more inclusive definition used by NSDUH.

Current smokers in that original analysis were identified as having smoked part of all of a

single cigarette in the past month, which effectively captures a broad range of smoking behaviors. This categorization likely overestimates cigarette use and confounds trends analysis across different demographic groups; for example, adolescents and adults.

The initial work identified menthol preference based on smoking a menthol cigarette in the last 30 days. This is not necessarily based on usual brand, although the earlier questions for that survey were based on usual brand.

So this is a figure that I think has got the attention of a lot of people with the interpretation that prevalence of menthol cigarette use among past month smokers decreases with age or that there is a preference among adolescents.

Again, smokers were identified as having smoked part or all of a single cigarette. This categorization combines both experimenting and experienced or established smokers, which are represented differently across the age groups.

So adolescents are more likely to experiment with cigarettes and that population would be disproportionately or at least heavily impacted that way, where adults are more likely to be established smokers and would likely have few experimenters. Therefore, it's difficult to take away any consistent conclusions from a trend analysis like this.

The data we saw at the last meeting was specifically looking at past month smokers based on a single cigarette. They did report one finding in the initial report based on daily smokers, and, as you see in the numbers, daily smokers were less likely than less frequent smokers to use menthol cigarettes, 30.1 versus 30.5.

So if you look at it from the perspective of the more rigid definition of smokers, the difference narrows quite significantly. And that data was available, but was not reported.

So in terms of what we did, we cast a broad net to look at the different national

surveys to see what surveys had information on menthol cigarette use. The four we identified were NHANES, NHIS, NSDUH, and NYTS. As it turns out, there have been some publications on each of these in the literature.

The NHANES offered us the opportunity to combine a couple years' data to increase our N. So we took advantage of that, using standard survey statistical methods. I've listed the population sizes. I'll point out that the NHANES and the NSDUH both allow an analysis of adolescents and adults. The NYTS is unique among the surveys in that the survey is conducted in a group setting, and I'll explain the ramifications of that in a few minutes.

The NSDUH is unique among the surveys in that past month use is defined by smoking part of all of a cigarette in the last 30 days versus usual brand use. We consider that a more inclusive definition. It is conceivable that someone could be a usual brand non-menthol smoker, but if, in fact, they've smoked a menthol

cigarette in the past 30 days, would answer affirmatively to that question.

So as we identified our surveys and tried to decide the most thoughtful way of identifying current smokers, we clearly didn't think that the broad range that's captured with an adolescent categorization of smoking was appropriate. Daily smoking seemed a bit rigid.

So we settled on smoking 10 or more over the last 30 days. This was our attempt to more closely identify established smokers. Again, the definitions used for adolescent smoking are all or part of a cigarette in the past 30 days. While this may be very effective for answering certain hypotheses, it's likely ineffective for identifying regular smoking.

Adults are typically identified as smoking at least 100 cigarettes lifetime and currently smoking every day or some days. So we viewed our definition as a fairly conservative approach at going after daily smoking.

As I mentioned before, adolescent

characterization captures a broad range of smoking behaviors. I think that was brought up at the last meeting by a presenter. We believe it's inappropriate for generating trend analyses, as I've already mentioned, and it overestimates regular smoking.

For example, the NSDUH data suggests that three-quarters of adolescents experimenting with cigarettes do not become regular smokers. If they, in fact, were looked at with the adult categorization, it's possible that a large percentage of those would be identified as never smokers.

So the initial conclusion from the March meeting was that menthol cigarette use is higher among adolescents than adults. We would argue the adolescent categorization, as was used, is not appropriate for trend analysis. And with the data that we've generated from the national surveys, we would argue that there's similar percentages of current menthol use among the different age groups, as long as properly and consistently

identify smokers and cigarettes type preference.

Also, current menthol cigarette use is statistically lower overall and for all demographic groups, other than non-Hispanic black.

So what these bar graphs represent is the percentage of current smokers that report menthol cigarette use. If the bar is colored, it was statistically different versus non-menthol cigarette use.

The NHANES and the NHIS indicate statistically lower percentages overall, these are unadjusted numbers, for menthol versus non-menthol cigarette use. These percentages were comparable and were similar to the TUS-CPS, which we used as kind of a reference to see if we were in the ballpark. Again, these data were based on usual brand.

The NSDUH provided similar findings, although slightly elevated in percentage. Again, this was based on a more inclusive definition of menthol cigarette use. The NYTS also suggested lower percentages, although they were markedly

higher than the other surveys; again, this survey specific to adolescents and is acquired in a group setting.

When we stratify the data based on gender, again, the NHANES and NHIS indicate statistically lower percentages. We see a lot of similarity across NHANES and NHIS and comparable numbers to TUS-CPS. Again, the NSDUH provides similar findings, with the percentages slightly higher. The males for NYTS are comparatively higher than the other surveys, and, hence, females do not trend higher than males anymore.

My apologies. Earlier, I should have stated that the females do trend higher than the males by about 10 percent in the first surveys and maybe 6 percent in the NSDUH.

When we look at race/ethnicity, and the way we looked at the data was non-Hispanic white, non-Hispanic black, and other. I'm not going to provide the "other" data, but all the data is available in the draft manuscripts that we provided the committee.

Again, the NHANES and NHIS indicate statistically lower and higher percentages for non-Hispanic white, non-Hispanic black. Current menthol smokers, the percentages are comparable and similar to the TUS-CPS, and there's about a three or four-fold difference in the percentages reported.

The NSDUH provides similar findings, while the NYTS, we have a significantly higher prevalence of use for non-Hispanic whites, 15 to 20 percent, and that causes the difference between non-Hispanic blacks and non-Hispanic whites to be somewhat attenuated compared to the other surveys.

So if you look across the surveys, we see a lot of similarities with the first three survey and some differences with NYTS. When you look at age, the NHANES indicates similar percentages of menthol cigarette smokers across age groups, with maybe a slightly higher percentage in the 18 to 24 years. We have more variability at the lower ages, given the lower number of respondents.

But you see that the percentage of

adolescents reporting current menthol cigarette use is 26.4 versus an overall number of 25.7 and comparable numbers. You'll also notice that our stratification on age was heavily weighted towards the younger ages.

For the NSDUH and NYTS, they have markedly higher percentages of adolescent menthol smokers. The NSDUH is based on a more inclusive criteria, and the NYTS is administered in a group setting. I'll talk about those things.

So the NYTS differs significantly in population, adolescents only, and collecting survey in a group setting. As was pointed out during the last TPSAC meeting, Giovono, et al, examined the accuracy of self-reported menthol versus non-menthol cigarette use and reported that 12 percent of respondents provide conflicting information on cigarette type, with those numbers being even higher for adolescents, although that number was reported.

Kann, et al, in 2002, compared the adolescent responses to 42 identically worded

questions from a school-based survey, the YRBS, and the household-based NHIS. There were higher risk estimates provided by the school-based versus the household-based setting on 39 of the 42 items, 93 percent of the items; 24 of those items were statistically different, including ever tried smoking; smoked whole cigarette prior to the age of 13; ever smoked regularly; and, smoked regularly prior to the age of 13.

Moving on to menthol cigarette use and smoking initiation age. From the earlier meeting, the presentation really did focus on the preference of menthol versus non-menthol cigarette use among new smokers.

There were two studies interpreted to suggest that beginner smokers are more likely to initiate using menthol cigarettes, a beginning smoker defined as someone who has initiated in the last 12 months versus a more experienced smoker that had initiated the year previous.

Neither study, in my understanding of the surveys, allows a reported initiation type

cigarette, only if menthol cigarette was used in the last 30 days or is it the current usual brand. Equally important, despite the focus on initiation, there were no data provided regarding recent adolescent smoking trends.

So let's talk about those two studies real quick. The NSDUH data suggests a trend for higher past month cigarette use among beginner smokers. What wasn't made evident is that 1.7 percent of past month smokers were categorized as beginners from the entire population and that further stratification for demographic analyses, coupled with the disproportionate comparator groups, in our mind, raises concerns regarding the strength and relevance of the findings. It's important to point out that the data could have been looked at differently, with different categorizations.

The Hersey, et al, 2002 paper had similar suggestions. Again, maybe not obvious to the committee when it was presented was that there was a disproportionate percentage of excluded data

from the beginner smoker population. The authors themselves caution against interpreting findings as suggestive of subsequent use. And an initial review by the Center for Regulatory Effectiveness suggests that this study has a number of shortcomings and may be noncompliant with the Data Quality Act.

So among adolescent trends, again, I've talked about what the NSDUH data suggests, based on part or all of a single cigarette in the past month versus usual brand. This survey similarly provides data on past month cigarette use and past year cigarette smoking initiation for the same period.

So if we look at male and female past month cigarette use, it is declining, with statistical reductions from year to year, all except for, I think, the last year.

It's also important to know that the prevalence of smoking among adolescents compared to adults is about half and the smoking prevalence among African-Americans compared to Caucasians is

approximately half. These would be based on government survey data.

Additionally, male and female past year cigarette use initiation has been unchanged from the period of 2002 to 2008.

So the initial conclusion was that menthol cigarettes are used as a starter product by beginner smokers, possibly reducing initiation age, at least that's the way it's been interpreted. We would argue that past month adolescent cigarette smoke use is declining, and past year smoking initiation is unchanged.

Moreover, we have data to suggest that current menthol smokers report statistically older initiation ages and that menthol cigarette use is associated with an older age for initiating daily smoking.

So the way these data are set up is this is smoking initiation age difference, menthol versus non-menthol. If the line moves to the right -- and I'm sorry about the imaginary line, but there is an imaginary line down the center.

If the bars move to the right, it is a statistically older initiation age for menthol smokers, if, in fact, those bars are colored green. If the bar moves to the left, it's a statistically younger initiation age for menthol versus non-menthol smokers. R stands for regular smoking, D-daily smoking, and F-first cigarette smoked.

So the NHANES and the NHIS suggest older initiating age for regular smoking, menthol versus non-menthol cigarette use. The NSDUH data provides similar findings based on both first cigarette smoked and age initiating daily smoking. And the NYTS suggests a younger age for first cigarette smoked for current menthol cigarette use. This is in stark contrast to the other three surveys. Again, this survey is based on adolescents only, with the survey being conducted in a group setting.

When we stratify by gender, here is the data for the males and the females, set up the same way. The NHANES and NHIS suggest older age

of initiating regular smoking for both male and female smokers. The NSDUH data provides similar findings, again, based on first cigarette and initiation of daily smoking. And the NYTS trends, again, suggest younger age of first cigarette smoked.

When we did this analysis on other stratifications, we saw no differences in average age of smoking initiation for non-Hispanic whites, non-Hispanic blacks, adolescents, or any of the younger adult categorizations.

When we looked at the age 30 and above, the NHANES and the NHIS suggest an older age of initiating regular smoking for adults age 30-plus, current menthol smokers. And the NSDUH provides similar findings, again, based on two metrics in the same survey, first cigarette smoked and initiating daily smoking.

So when we take these data and do regression model analysis, in the draft manuscripts that were provided to the committee, all the data from all the different strata are in

the manuscripts, as are all the regression model results, whether we did it with a single variable or combined variables.

The manuscripts, I think, encompass about 32 tables, fairly complex. And I couldn't present all the data, so I tried to distill it down to what I thought would be most informative.

So what we have across the top is the unadjusted data, which I've already showed. And the way these are provided is the average non-menthol smoking initiation age minus menthol smoking initiation age. So that the negative sign actually indicates an older initiation age and is in green. The red is a younger initiation age for the NYTS.

So the NHANES, the NHIS and the NSDUH indicate current menthol cigarette smokers report statistically older initiation ages, again, on three different metrics; first cigarette, regular smoking, and daily smoking. And the NSDUH data indicates that menthol cigarette use is independently associated with an older age for

initiating daily smoking when we control for gender, race/ethnicity, and current age. We did not attempt to control for any socioeconomic factors. This work started in December and we just haven't had an opportunity to go that far yet, but we do believe those factors are important. Again, this is in stark contrast to what you see with the NYTS.

The data I'm presenting so far is cross-sectional analysis of the most recent data we could get from these surveys. We're not in a position right now to do longitudinal analyses, but what we have done is started going down the path of looking at these surveys and what they can provide us in a multiple year analysis.

We have finished that analysis for NHANES from 2000 to 2008, and we'll call this a time trend analysis. What we're looking at here is initiation for adolescents, because while initiation age is important, I think all of us would rather have initiation rate data.

What we see is no statistical difference

over time in smoking initiation rates when the data are unadjusted, and we have a slight decline in smoking initiation rate for adolescents, current menthol and non-menthol smokers both. There are no statistical differences here. And this data is very similar to what I've already presented from the NSDUH. Again, this data is from the NHANES, which based current cigarette preference on usual brand.

So menthol cigarette use and smoking dependence. You heard during the initial presentation in March that night waking to smoke was a preferred metric for dependence, and a single study, Bover, et al, was provided as evidence that menthol cigarette use is associated with greater smoking dependence.

There's a similar paper that wasn't discussed, Gandhi, et al, 2009. These papers have similar conclusions, but they were both based on generally the same cohort, and, that is, consecutive patients from a cessation clinic, with a large overlap in those consecutive patients.

What wasn't discussed or clear was that there were 14 variables associated with night waking to smoke, making it very difficult to determine any independent effect of menthol smoking due to inter-correlations. And we would argue that findings from populations of treatment-seeking individuals in smoking cessation trials are likely not generalizable to the entire population.

If I was up here telling you about data from a smoking cessation trial that involved white males over the age of 50, I think I would be challenged to make inference that that has anything to do with adolescent smoking.

Time to first cigarette was also suggested to be a better metric for dependence, and three studies were cited as supporting an association for greater smoking dependence. The Bover, et al, paper, if you read it closely, there is no association between menthol smoking and reduced time to first cigarette, although both are independently associated with night waking to

smoke.

The Collins and Moolchan paper reported statistical differences based on less than five minutes time to first cigarettes, but no differences based on six to 30, 31 to 60, or greater than 60 minutes. While this field is new to me, my understanding is that the preferred metric is plus or minus 30 minutes.

Then, again, findings from populations of treatment-seekers in smoking cessation trials, again, most people who quit smoking without intervention are likely not generalizable to the entire population. All three of these studies represent those type of populations.

Five additional studies were not discussed. Three of those were from cessation trials. Those also included a large survey from the COMMIT, Hyland, et al, 2002, which indicated increased time to first cigarette and, therefore, reduced dependency for menthol smokers.

The Fagerstrom test for nicotine dependence or a similar type dependence score,

findings of no difference were interpreted as providing insufficient supporting evidence for a conclusion. My sense is that there were only two papers, because we saw conclusions based on one paper. But we would argue that these data suggest that menthol use is not associated with increased smoking dependence.

There were five additional studies not discussed. Again, I think three of them were from a smoking cessation trial. The lung health study by Murray, et al, in 2007 indicated no differences for smoking dependence, while the NYTS has provided some mixed findings.

Wackowski and Delnevo reported increased dependence for adolescent menthol smokers on two of four questions, but failed to report an overall dependency score.

Then the Hersey, et al, paper suggested that adolescent smokers were more likely to report a higher dependency score, but at the same time, statistically less likely to report smoking on 20 or more of the last 30 days or to have smoked more

than six cigarettes per day. Again, this study is under review.

Cigarettes per day was also argued to be a less informative metric. We would disagree, given its relevance to exposure. The findings of reduced smoking intensity in two studies, and no differences were, again, interpreted as providing insufficient supporting evidence for a conclusion.

We would argue that these data, particularly Muscat, et al, which looked at a number of different metrics, suggest menthol cigarettes use not associated with increased smoking dependence.

There were six additional studies that were not discussed, including large population studies that indicated either no difference or reduced dependency, respectively.

Then the Muscat, et al, 2009 recent report suggested that cigarettes per day, time to first cigarette, and the Fagerstrom score or similar score are equally correlated with plasma and urinary cotinine, which serves as an exposure

biomarker.

So from the initial meeting, it was suggested that menthol use is associated with increased smoking dependence. We would argue that the cited published literature is insufficient to support this conclusion and may even suggest a reduced dependence.

Moreover, the results from our national survey data suggests fairly convincingly that current menthol smokers report statistically lower smoking intensity and that menthol cigarette use is independently associated with a lower smoking intensity.

So the way these are laid out is this is a difference in cigarettes per day, menthol versus non-menthol. Again, if the bar is colored, it's statistically different. And if it's moving to the left, it represents fewer cigarettes per day for menthol versus on-menthol cigarettes.

So in the unadjusted data, you see that menthol smokers report an average of between 2.5 and 3 cigarettes or approximately 2.5 and 3

cigarettes fewer than non-menthol smokers.

There were no statistical differences for non-Hispanic blacks or adolescents, but when we stratify by gender, you see that there are differences for gender, especially in the NHIS, which has twice the population size. You're talking about 3 cigarettes per day for males fewer for menthol versus non-menthol smokers, about 1.5 for females, and about 1.5 for non-Hispanic whites.

When you look at age effects, you see, again, in the NHIS, which has the largest dataset for the continuous data that we are able to analyze, 2 to 2.5 fewer cigarettes per day across the age groups for menthol versus non-menthol cigarette smokers.

When we do regression analysis, and the unadjusted numbers are at the top, I didn't show you data from the NSDUH and the NYTS, because that was categorized data and we didn't look at it that way.

So what you have for those points is an

analysis of categorized data, the unadjusted. All the stratified data are in the draft manuscripts. There were a number of differences in the stratified data.

What you see here is for the NSDUH, a 40 or 45 percent lower odds of being associated with the middle or high intensity smoking categorization if you're a menthol versus a non-menthol smoker. The NYTS, again, as everything we've seen in our analyses, gives the opposite results, and hat would be an increased odds of being associated with those categories if you're a menthol smoker.

The NHIS data, which is the largest database -- largest survey to provide continuous data, suggests that menthol use is independently associated with lower smoking intensity. The p-value is .06, very close to statistical significance. And, again, these data are markedly different from the NYTS.

So menthol cigarette use and attempted quitting. Review of selected publications were

interpreted to suggest during the March meeting that there was no effect or lower smoking cessation associated with menthol cigarette use. It was also suggested that there was limited data for a possibility of an interaction between race/ethnicity and menthol in terms of poorer cessation outcomes.

A large proportion of the cited studies were based on, again, study populations from smoking cessation trials, which we believe are not generalizable to the entire population, especially when population data are available for this type of analysis, which we're attempting to demonstrate today.

Additionally, results from these type studies generally constitute unadjusted analyses and use different definitions for or durations to assess cessation success. For example, studies would range from four weeks abstinence to five years abstinence and provide varying results in different studies, making it very difficult to discern anything from those studies.

So as we look at this data, and there's quite a bit of it, we look at the data in three buckets, if you will. One is national survey data, which we believe is more representative to the entire population; the second would be results from larger surveys that look at spontaneous smoking cession; and, the third would be from the smoking cessation trials.

There was one study by Gundersen based on national survey data and is particularly relevant here, since we also looked at the NHIS. They reported a recalculated adjusted odds ratio that suggested that menthol use was associated with decreased cessation for non-whites -- non-whites is the collapsing of African-Americans and Hispanics -- while an increased cessation for whites. Both those differences were statistically significant.

The findings of no difference, statistical increases, and/or statistical decreases for the same demographic group seemed to be dependent on the analytical approach used; that

is, the use of interactive terms and/or demographic grouping, as I've pointed out.

Prior to the recalculations, statistically higher success for whites was noted, statistically lower success for Hispanics, with no statistical differences for blacks.

The data do not provide evidence of an independent association for menthol cigarette use and reduced smoking cessation. In my mind, they instead point to a socioeconomic variable which has yet to be accounted for.

When we look at the disease risk or like populations, the second bucket I talked about, I will not talk about all these studies, but hopefully you can see what's highlighted in the yellow there. The findings from these large population surveys examining spontaneous smoking cession we believe may be more informative, and they overall do not suggest an association with menthol cigarette use and reduced smoking cessation.

I will not talk about the smoking

cessation trial studies, for the reasons I've already stated. We do not think they're generalizable to the entire population.

The conclusion from March was that there was no effect or a lower smoking cessation success associated with menthol cigarette use. We would argue the findings from representative studies do not suggest an association, and that there is a statistical increase for the percentage of adult menthol smokers reporting a cessation attempt in the last 12 months -- this is how we looked at the data -- and that there is an increased odds of attempting to quit among menthol cigarette smokers. When we also looked at this question in adolescents, there was no difference.

So the NYTS I've already pointed out is an adolescent-only survey. The NHANES only asks this question of whether you've attempted to quit in the past 12 months of the adolescent population.

When you look at the data, there is no difference, statistical differences in

percentages. Hence, we did no regression model analysis.

When you look at the data from NHIS, which is an adult-only population, you see a statistical difference, with more current menthol smokers reporting a cessation attempt in the last 12 months versus non-menthol current smokers. When you do regression model analysis, you see that this statistical difference holds all the way through to the combination of gender, race/ethnicity, and current age, suggesting that there's an increased odds of recent quit attempt among menthol smokers and it's independently associated with menthol smoking.

So menthol cigarette use summary. The published literature on population level effects, menthol versus non-menthol cigarette use, is largely insufficient to support an evidence-based conclusion. This is based on a lack of standardized metrics, how you identify current smokers, how you determine menthol cigarette use, and outcomes associated with initiation dependence

and cessation. For example, what metrics do you use for dependence? And if you were to look at time to first cigarettes, what time do you use? When you look at cessation, do you define it at four weeks, at six months, at five years?

There's also limited generalizability for many of these studies to the entire U.S. population, and there has been an inadequate analysis of adolescents, given that that is a primary focus.

When we look at menthol cigarette use among current smokers, based on usual brand, not smoked in the past 30 days, which is much more inclusive, of current smoking, not smoked part or all of a cigarette in the past 30 days, the survey data indicate no age-related trend for menthol cigarette use adolescent versus overall, which may, in some ways, address some of the inconsistencies that were discussed yesterday afternoon regarding the switching data.

The survey data also indicates statistically lower percentages for current

menthol smokers, unadjusted, and for both genders, with a trend of females being higher than males by about 10 percent for non-Hispanic whites and for all age groups. A statistically higher percentage of non-Hispanics blacks report menthol cigarette use and this difference between non-Hispanic black and non-Hispanic white is significant, three to four-fold.

So we view individual risk and population risk as associated. And so I've got this schematic that looks at these two things and summarizes the data. As you heard yesterday, there's been at least 13 epidemiological studies examining the disease outcomes associated with menthol versus non-menthol cigarette use, and the metrics they have looked at are included there.

Twelve of these studies reported no significant differences in disease outcome. The one study that did, the effect was not seen in females, only reported in males, and was later called likely a mere chance finding by the same authors.

Importantly, two recent studies suggest the risk for lung cancer may be decreased for menthol versus non-menthol cigarette smokers; specifically, a report from the Spitz Lab on an African-American specific model for lung cancer and a meta-analysis from the available studies done by Werley, et al. This is consistent with what you heard in the really nice presentation on the TES study yesterday on exposure.

But is there biological plausibility for this? So the NHANES, NHIS and NSDUH data indicate menthol cigarette users report statistically older average initiation ages, and it's independently associated with an older initiation age for daily smoking.

The same surveys indicate menthol cigarette users report statistically lower smoking intensities, again, independently associated with lower smoking intensity when you look at the continuous data from the NHIS. Also, as a reminder, the metrics for dependence that are customarily used seem to be equally correlated

with biomarkers of exposure.

Then, last, the NHIS data indicate menthol cigarette use among adults is independently associated with an increased odds of recently attempting smoking cessation, while the other two surveys suggest no difference for adolescents.

Government survey data, therefore, indicate no adverse population level effects associated with current menthol versus non-menthol cigarette use; no age-related differences in the one survey we looked at, which properly defines some of the metrics; older average age of smoking initiation; lower average smoking intensity; and, a higher percentage of adults attempting smoking cessation.

We would clearly like to have more data on initiation rate and cessation success, and we're attempting to do that through our multi-year analyses of some of these surveys. Therefore, we contend that the data indicate no scientific basis to regulate menthol cigarettes differently than

non-menthol cigarettes.

Thank you.

MS. HUNTER: Good morning. My name is Jennifer Hunter. I am Vice President, Corporate Affairs for Altria Client Services. Since 2005, I've had leadership responsibility for PM USA's efforts to prevent underage cigarette smoking.

Today, my remarks will focus primarily on menthol and initiation. First, as you heard yesterday, kids should not smoke menthol or non-menthol cigarettes. Underage smoking is a complex issue. There is no single reason why kids engage in risky behavior like cigarette smoking, and a comprehensive approach to addressing the behavior is necessary.

It's been reported that underage smoking rates have declined since peak years in the late 1990s. While we're encouraged by this progress, additional efforts to help reduce and prevent underage smoking remains an important priority.

Based on our review of the limited literature and data available, we have concluded

that menthol does not play a unique role in the initiation of cigarettes. PM USA and others have an important role to play in helping to prevent underage cigarette smoking. Philip Morris USA has over 10 years of experience trying to understand why kids smoke cigarettes and identifying and supporting programs and legislation, like FDA regulation of the tobacco industry, to help prevent underage smoking.

As we have looked at menthol specifically, we've relied on some of the same information that you all looked at at the March meeting, with studies and data related o menthol and cigarette initiation; specifically, underage smoking trends, age of initiation, reactions to first smoking experience, and recency of initiation.

So I'd first like to start with underage smoking trends. As we take a broad view, first, of underage smoking, as I indicated, it has been reported that underage smoking has declined since reaching peak levels in the late 1990s. This

information is monitoring the future.

What you can see from the data are decreases across 8th grade, 10th grade and 12th grade. These findings are consistent with other national studies, like YRBS and NSDUH.

This slide shows the total estimated numbers and percentages of past 30-day cigarette smokers by age. This information is from NSDUH. What you can see here is that 96 percent of those reporting smoking are above the age of 18.

Now, as we look specifically at menthol and reported rates of use, NSDUH has reported a higher rate of menthol use for underage smokers. Again, they've relied on -- well, this is NSDUH data. What we have seen, however, is that between 2004 and 2008, when the percent of reported smoking showed an increase, the estimated number of smokers has actually declined from 1.2 million in 2004 to 1 million in 2008. What we also have seen is with this dataset, underage smoking showed a decline from 11.9 to 9.1.

Now, as we look specifically at African-

American underage smokers, NSDUH indicates that menthol smokers report a lower rate of use than their white counterparts. And in another study, African-Americans report starting cigarette smoking at a later age than white smokers.

Now, as we look at age of initiation and reactions to initial smoking experience, studies suggest no difference in age of initiation between menthol and non-menthol smokers. Jeff just presented some of this information. These were studies that were focused on cessation that had baseline information on age of initiation, and there was no reported difference between menthol and non-menthol.

As we report from one study, DeFranza, et al, in 2004, he found that reactions to initial smoking experience do not differ between menthol and non-menthol cigarettes.

Again, this is information that you all reviewed at the March meeting. This slide is intended to highlight the data that were presented in the DeFranza study. What you will note is

there is no statistically significant difference between irritation, nausea, dizziness, or relaxation between menthol or non-menthol smokers, nor do you see a difference between future intention to smoke.

Now, finally, as we look at recency of initiation, there were two studies, Hersey, et al, and SAMHSA 2009. These two studies have suggested that there is a higher likelihood of smoking initiation of more recent smoking initiates. Both of these studies relied on national survey data and they looked at current year initiates versus prior year initiates.

What they found is that current year initiates had a greater likelihood to have a higher reported rate of use of menthol than the prior year initiates.

Now, at the March meeting, you all had a conversation about the change to the NSDUH survey question in 2004, and there was a question that was raised about what the measure currently is, usual use or any use.

So in order to understand that question and the conversation you all had, we performed some additional analysis, looking at current year and prior year initiates. This slide shows the data from 2000 to 2008. This is looking at 12 to 17-year-olds, current year initiates versus prior year initiates.

If you look at the 2000 to 2003, the survey question was "During the past 30 days, did you smoke menthol or regular cigarettes most often," and they have to select menthol or regular. These data indicate that current year initiates have a lower reported rate of menthol use than prior year initiates.

In 2004, when the question changed, it now reads "Were the cigarettes you smoked during the past 30 days menthol, yes or no?" These data show that current year initiates, in most years, have a higher reported rate of menthol use than prior year initiates. So as we look at across this timeframe from 2000 to 2008, we see two different patterns of data.

The point of showing this is not to poke at NSDUH. It's really to highlight the importance of how we ask the question so we're clear on what we are assessing as it relates to menthol, usual use of menthol or any use of menthol.

So as we look at the information we've covered so far, underage rates, age of initiation, recency, reaction to first cigarette smoked, we don't believe that menthol plays a unique role in initiation.

But what's going on? So we've looked at why kids smoke, how they get access to cigarettes, and what can be done about it. So as we first look at how kids are getting access to cigarettes, the landscape really has changed over the last several years.

This information is from Wyer BS. It assesses how high school students have reported gaining access to cigarettes, and its usual source of access. In 1995, you can see that the primary source of access were commercial sources. They were going to retail, they were buying cigarettes.

In 2009, the primary source of access that's reported is now social sources. So what is the impact from menthol, as kids are relying on other individuals in order to get access to their cigarettes? There are two products that are available in the marketplace, menthol or non-menthol. There is a likelihood that they could have some experience with menthol.

As we look at the progress, though, that's been made between commercial source and social source, this also raises an opportunity for the agency really to try to understand social sources and identify ways in which to address this new landscape that we face.

But why do kids smoke? As I said earlier, there is no single reason why kids smoke. This is a complex issue that has personal, social and environmental factors that contribute to this.

There is a rich body of literature. In 1994, the Surgeon General reported that there are sociodemographic, environmental, behavioral, and personal factors that can encourage the onset of

tobacco use among adolescents. This view has not changed.

Last week, the CDC issued a report and they also highlighted the personal, social and environmental factors that can contribute to a kid's decision to use cigarettes. Menthol has not been identified as a unique risk factor.

But what can we do? An approach to addressing this issue really focuses on positive use development. How do we focus on this broader issue of kids smoking and focus on reducing the risk factors in a kid's life and increasing protective factors, making sure kids have positive peer relationships, they are connected with their parents, they have other caring adults in their lives.

They've been exposed to life skills that can help them make better decisions about risky behaviors. We've limited access to risky products and they've got constructive activities. This theory suggests that having kids with more protective factors will be able to make decisions

and avoid a broad range of risky behaviors like tobacco use.

So as we've looked at this information, underage smoking rates have declined since peak levels in the late 1990s. As I stated, based on our review of the limited available literature and data, menthol cigarettes do not appear to play a unique role in smoking initiation. However, underage smoking continues to be a very serious issue, menthol and non-menthol. Additional prevention efforts continue to be a priority, and PM USA and others have an important role to play.

I'd like to leave you with one last thought. There are programs that are currently available. I mentioned life skills and protective factors. I raise this just as an example of a program that has been implemented in middle schools. It's proven outcomes across a broad range of risky behaviors, like tobacco, alcohol and drug use.

In fact, they report decreases in weekly smoking by up to 87 percent of students who have

participated in all three years of the program. It's been proven effective across a broad range of students. It has long-term effects, and it's cost-effective. And finally, this is a program that's been endorsed by a number of organizations.

Thank you for your time.

DR. TRUE: Good morning. My name is Bill True, and I'm the senior vice president of Research and Development for the Lorillard Tobacco Company. And I'd like to finish up this section with a brief discussion on population effects.

We just heard some of the challenges and limitations of the survey data and the impact on trying to answer some questions about youth smoking. For example, in the survey that's most often used, there's ambiguity around the question of the type of cigarette smoked. It definitely allows for some opportunity for double-counting and fails to account certainly for that mixed use.

As we know, three out of four youth experimenting with cigarettes do not continue on to a regular smoking habit; and, certainly, these

studies are capturing youth at various phases of experimentation.

So in order to address looking at this question from a different approach, we were curious about is smoking related at all to the local menthol prevalence in terms of availability, since we just saw a chart on how youth typically access their cigarettes.

So we wanted to determine whether a correlation existed between youth smoking rates and menthol market share. And what we found was that youth smoking rates are generally lower in states with higher menthol market share. Youth smoking appears to be inversely related to menthol market share.

This is a little bit of a busy graph, but it just shows the data. The bar on the left, or in blue, if it's legible to you, is the menthol market share; and the bar on the right, or red, would be the youth smoking rate on a statewide basis. And as you can see, a number of states, I believe 25 to 27, clearly, have significantly

higher than average market share of menthol, yet lower than average youth smoking rates.

If we look at a scatter plot and take these individual states and we superimpose, averages lines would be the red lines, of the average youth smoking rate, horizontally, at 19.5 percent and the average market share of menthol, 28.9 percent, you get these quadrants to evaluate.

As you can see, on the left-hand side of this chart, you see a number of states that have significantly lower market share of menthol, yet have some of the highest youth smoking rates.

Further, there is no data that we've been able to find or have been provided by anyone else to suggest that restricting or eliminating menthol would have any effect on a youth's decision to smoke.

On to a new study that was recently conducted and will be published recently on a meta-analysis of the lung cancer studies that have been done to date for cigarette smoking. A draft manuscript has been provided and we will submit

that draft manuscript, as well as the final manuscript as it's presented.

The study is a meta-analysis, which means it takes all of the data that was developed across the epidemiological studies relative to lung cancer and looks statistically at that information. This does include eight specific studies.

The findings, if you look across these various subgroups, show that the relative risks all range between .9 and 1.0. And the interesting question that was posed by the author was in trying to explain the increased lung cancer risk for African-American men. It's been calculated it would require a relative risk of 1.7 to 1.8 in order to explain that.

The conclusion of the study is that their increased lung cancer risk cannot possibly be explained by the much greater preference of blacks for mentholated cigarettes.

In conclusion, there is extensive and conclusive data on the health effects of menthol

cigarettes. The major manufacturers have done their best to provide the information requested by TPSAC not only through the presentations over the past two days, but with hundreds, potentially thousands of pages of submissions and extensive bibliographies of relevant published studies.

In addition, an extensive document production has already been made to the FDA. Another one will be made in August, and detailed product information has been submitted to the FDA in June.

The committee says it needs more data. Thirteen epidemiological studies, the gold standard of evaluating disease risk, the largest cigarette biomarker study ever conducted in Philip Morris USA's total exposure study, with over 3,600 smokers, over 10 times the number of smokers in any other study typically done in this area.

As we've seen, three out of the four national surveys show no effect on menthol initiation, dependence, or cessation. The data is overwhelming and consistent. Menthol has no

effect on the health risks of smoking; or is this committee adopting a standard that requires more than 13 epidemiological studies and biomarker studies of more than 3,600 participants to come to any conclusion on any health issue related to cigarettes?

The process of evaluating the health effects of menthol seems to have begun with an underlying presumption by several committee members that menthol must have some adverse effect. And despite all of the evidence to the contrary, these members keep searching for some data that might support their presumption.

The undercurrent of this notion appears to be preventing this evaluation process from being truly science-based and data-driven. Science must be dispassionate. When the data doesn't support the hypothesis, the hypothesis must be abandoned. That is the scientific method; that is sound science.

Thank you.

DR. SAMET: Thank you for your

presentations.

We're going to move on now to 30 minutes of clarifying questions. Just as a warning, I'm starting right. And let me ask, how many will have questions? Just to get a sense. Okay. And I'll start with Dan, and moving on to John, Arnold, Susan.

No. Ursula?

DR. BAUER: A question for Dr. Hunter. I'm looking at, I think, slide 12, your positive youth development.

Would you clarify? Is it the position of Philip Morris USA that price and marketing have no influence on youth initiation?

MS. HUNTER: No. Our intent is to make very clear that, again, there's no single reason why kids smoke cigarettes. There are a variety of factors that do contribute to kids smoking. The positive youth development approach really is intended just to highlight a variety of things that really can protect for kids, give them the positive support that they need, develop their

thinking to help them avoid a broad range of behaviors.

So there are a variety of factors that contribute to underage use of smoking.

DR. BAUER: So where do price and marketing fit in terms of overall importance in influence initiation?

MS. HUNTER: We would agree that price and marketing, like some of the other factors, like parents smoking, peers smoking, siblings smoking, play a role in kids' decisions to initiate. So, again, there is no single reason why kids smoke. There are a variety of contributing factors.

You mentioned marketing and pricing. We have worked to limit our marketing visibility. I think you heard Mr. Fernandez yesterday talk about the fact that we have not been advertising in magazines. We've reduced our visibility at retail.

So we do understand that there is a role that that can play and we've really tried to work

to address that.

DR. BAUER: And for Drs. Curtin and True, based on your analyses of the variety of datasets and what you presented today, do you conclude that youth who experiment with menthol cigarettes are less likely than you to experiment with non-menthol cigarettes to progress to established smoking?

DR. TRUE: I would say that Jeff has a much more thorough and conclusive evaluation of that information. However, I believe my interpretation of that data would suggest that there's no difference between the non-menthol and the menthol.

DR. CURTIN: Could you repeat the question again, to make sure I understood it?

DR. BAUER: Sure. Based on your analysis of the data, would you conclude that youth who experiment with menthol cigarettes, as opposed to those who experiment with non-menthol cigarettes, are less likely to progress to established smoking?

DR. CURTIN: I don't think we can say that with evidence, anything we've developed. What we looked at was smoking initiation, dependency, and intent to quit or an attempt at cessation.

What we reported is that menthol cigarette use is associated with lower population effects. I think there is some data that you can look at. For example, it appears that there doesn't seem to be a difference in cessation success or maybe even initiation among the different demographics, and there seems to be different demographics on menthol use.

Those would be very indirect associations, which you could develop some hypotheses, but I don't know that we looked at that directly, other than to point out that surveys that do capture all experimenters are likely inappropriate for making conclusions on established smokers.

So I don't know if that helps at all.

DR. SAMET: I think, actually, Ursula, we

should tuck your question away, because I think from what we know about trajectories of smoking across adolescents, the question is whether there are actually any cohort studies that capture the information that you're looking for.

I think those are data that we would want to look for, if available, and I think it's something we'll come back to in our general discussion. Clearly, cross-sections are limited, not tracking individual smokers.

DR. CURTIN: We don't really have the opportunity to do longitudinal studies, but that's likely how something like that would have to be addressed. And I think as you read the available literature, a lot of people are calling for those studies, but I don't know of any studies that have been done that track a smoker long term or someone experimenting long term.

DR. SAMET: Right. There are a number of cohort studies of smoking across adolescents. The question is whether menthol use has been captured in those studies, which is evidence I think this

committee should look for.

Cathy?

DR. BACKINGER: I had two questions.

Do you want me to just ask one right now?

DR. SAMET: If they're quick.

DR. BACKINGER: Okay, if they're quick.

The first one for Dr. Curtin. You focused on, I think --and this is what I need clarification on. I think you were emphasizing that it's more important to look at past 30-day smoking versus smoking part of smoking a few puffs or part of a cigarette, and then I think you also were focusing on age of initiation as important factors.

So I'm just wondering whether -- this kind of gets back to maybe something Ursula was alluding to, which was experimentation and whether you feel or whether Philip Morris feels that it's important to then also look at experimentation, not just regular smoking, as a factor of menthol versus non-menthol.

DR. CURTIN: So in terms of past month

cigarette use, the argument we are making is that it is more appropriate to use a definition that's closer to adult smoking or regular smoking, and that is 10 or more over the last 30 days versus only smoked a single cigarette in the last 30 days.

DR. BACKINGER: And why, given that youth are much different in their smoking trajectory and their smoking pattern and history compared with adults?

DR. CURTIN: I think that it is inappropriate to make decisions on smoking behaviors if someone has single puff of a cigarette versus they're actually picking up and smoking.

That's why we didn't use daily smoking as our metric. We wanted to be able to capture some data on adolescent smoking. We didn't use 20 of the last 30 days, which, as I talked about, some data did, like the Hyland study. We backed all the way up to 10 days in the last 30 days.

As far as in the last 30 days, I think

that's the metric that's standardly applied versus did you smoke at all in the last year. Clearly, you could increase your N size, but if you were looking at did someone smoke one or part or all of a cigarette in the last year, you really couldn't track anything.

What was the rest of your question? I'm sorry.

DR. BACKINGER: That was my question. Then the other one is quick. This is for Jennifer Hunter.

I think it's slide number 9 where you were looking at the change in questions on NHSDA, and you mentioned that you thought -- you said that the questions we ask are really important. And we saw a change in pattern here on that slide.

But you didn't state which one you thought more accurately reflects menthol use of those two questions posed, and I wanted to hear what you thought about that.

MS. HUNTER: As we look at that slide and see the two different patterns emerge, I think

it's probably for others to try to determine which is the better question to ask. However, I raised the fact that you do see something different.

The question that gets to menthol or regular, where it's a choice, someone has to state that they have used a menthol or that they have used a regular cigarette. That really could get to usual use.

If you look at how Mr. Fernandez presented some of his information yesterday, they use a question construct for adults that's very similar, which says a menthol or the non-menthol cigarette. So again, they're having to make a choice.

When we look at a yes/no with menthol, we could be getting any use. So anyone who is experimenting or relying on social sources in order to access, we could actually be capturing individuals who have used both menthol or non-menthol cigarettes in that 30-day period.

So I think it's just something to look at. And also, in order to understand if it is a

better question, we'd have to look at misclassification data, as would as non-response data across age groups and smoking behaviors to really understand that.

DR. SAMET: Let's move on.

Mark?

DR. CLANTON: My question is for Dr. True, Bill True. On the menthol and lung cancer slide, the new Lorillard-sponsored meta-analysis, can you give us the eight studies that were used in this unpublished paper?

DR. TRUE: I can provide them for you. I don't have them with me.

DR. CLANTON: The FDA probably needs the data, as well, from those studies, the raw data to recalculate those relative risks.

So a question on relative risk. If I read this unpublished, non-peer-reviewed data correctly, the relative risk for smoking menthol cigarettes and lung cancer is, at the lower range, protective against lung cancer in blacks.

Is that correct? Relative risk of .84,

that would imply a protective effect, right?

DR. TRUE: Yes.

DR. CLANTON: And at worst, a 2 percent increase in lung cancer, according to these data, 1.02. DR. TRUE: Yes.

DR. CLANTON: So if you sort of average that out, menthol cigarettes, in these data, imply about a relative risk of one, which means there's no association between menthol cigarettes and lung cancer, according to these calculations.

Would that be correct?

DR. TRUE: That would be correct.

DR. CLANTON: Just stepping through the data, African-Americans principally smoke, at the 70 to 75 percent level, menthol cigarettes.

Is that correct?

DR. TRUE: That's correct.

DR. CLANTON: African-Americans suffer the highest incidence and death rate due to lung cancer. Do you dispute that?

DR. TRUE: No.

DR. CLANTON: But these data imply that

there's a protective effect for those who smoke menthol cigarettes against lung cancer.

DR. TRUE: I didn't say they implied there was a protective effect, because there is not statistical significance in that number.

DR. CLANTON: Thank you.

MS. DELEEUW: This refers to that same slide on menthol use by 12 to 17-year-olds. Do you know what the difference in the "don't know/refused" rate was between the two questions?

MS. HUNTER: I believe that information is in the submission. However, we saw that the rate appeared to actually double. But I would refer you back to the submission where that information can be found.

DR. SAMET: Neal, do you have a question?

DR. BENOWITZ: I've got a couple questions. One is that there were so many analyses presented that I had a hard time determining where there were adjustments for race and not for race in the menthol versus non-menthol, and that's important, especially for age

of initiation, because we know African-Americans, in general, start later and there might be other behaviors.

So to me, it would be really important to see the analyses really done separately by race, because I think that's the appropriate comparison to look at the menthol effects within white smokers and within African-Americans.

I think some of the analyses may have been controlled for that, but I'm not sure.

DR. CURTIN: In many of the analyses we looked at, whether it was smoking initiation age or smoking intensity or attempted cessation, a lot of data was shown where the data were stratified. The unadjusted data were stratified by race/ethnicity.

In many of the regression models, where we would have only controlled for race or we would have controlled for race along with age and gender, either individually or together, all those data are in the draft manuscripts we provided.

What we chose to show is if we controlled

for all demographics, what were the findings then. I don't minimize the importance of your specific question. We originally had all that data on one slide and it was just overwhelming. I don't know if you could have seen it from where you're sitting, because it's just so much data.

But the tables are available in the draft manuscripts, along with all the raw data on the correlation evaluations. As I mentioned, it's about 30 different tables. So I can't speak effectively to exactly what was going on with that particular demographic.

But we did see a number of independent effects for menthol; that is, older average initiation age, if it's based on daily smoking; fewer cigarettes per day if it was based on continuous data; and, an increased odds for adults attempting cessation in the last 12 months.

So those are situations where we actually did control for race, gender, and current age.

DR. BENOWITZ: And just to follow-up, for Dr. True, when you presented the data on menthol

market share compared to youth smoking rates, that clearly is confounded by race. So it's very difficult for me to accept the conclusion that this is a menthol effect versus a race effect.

I think your figure really should be, if possible, broken out by the racial -- percentages of, say, African-American versus non-African-Americans within each state.

DR. TRUE: I think, ultimately, our conclusion with this is that we can't attribute, in any way, shape or form, that by reducing menthol use or menthol prevalence in a particular area, that that's going to lead to lower youth smoking.

We looked at this as an alternative way of looking at data that exists that's readily available that would complement the analysis that you would get from these survey studies.

DR. BENOWITZ: But if white smokers start smoking earlier and African-American smokers smoke later and you're lumping them together and you're trying to look at youth smoking menthol versus

non-menthol, it's really not going to give a good picture.

So it would be nice if you could just redo that figure with a breakdown, trying to control for the state's population of African-Americans versus whites. It would be much more informative.

DR. TRUE: Sure.

DR. SAMET: Actually, Neal, just to follow-up, I think some of these same datasets will be looked at by FDA, as I understand, and I think there are general issues around when one might be interested in adjusting for some sort of national level estimate, when, in fact, there's so much heterogeneity by racial/ethnic groups that these analyses are only useful for certain purposes, which I think is what you're really getting at here.

I will point out, if you look through the submission, the manuscripts do have a great deal of detail, as was mentioned.

DR. TRUE: And I think our position,

Dr. Benowitz, would be that if you look at the complexity of these surveys or the complexity of trying to conduct the analysis to get at some of these underlying issues, we're not confident that we'll find all the information to be able to do as detailed and precise an evaluation as you and we would desire.

So just looking at what is available and trying to consider looking at it from different angles would be the approach that we take here.

DR. SAMET: Melanie?

DR. WAKEFIELD: I think adjusting for race is pretty basic, though. That's not complicated.

A couple of the questions I was going to ask have been asked by others. So I really just have one further one, which is for Philip Morris. So much was made about the question change and the comparison between the periods, and that's really why Dr. Rising, in his presentation, focused on 2004 and thereafter.

In the presentation in March, he showed

that the trends in menthol cigarette use amongst path month smokers, adolescent smokers, are increasing. Does Philip Morris dispute that that's happening?

MS. HUNTER: No. And in the presentation, we highlighted the fact that from 2004 to 2008, when there is a reported rate of use of menthol that's increasing -- I believe it goes from 43 to 48 percent -- that during that same period of time, when you look at the estimated number of smokers, youth smokers, that the number actually declines from 1.2 million to 1 million.

DR. WAKEFIELD: Among those youth who smoke, there's an increasing percentage who smoke menthol.

MS. HUNTER: The 1.2 million to 1 million are those that reported using menthol. So when you look at the percent change from 2004, which was 43 and some change to 48 percent in 2008, when you look at the estimated numbers of kids in --

DR. WAKEFIELD: I'm asking for the percentage and if you think the percentage has

increased, and I think you just said, yes, it has. Thank you.

DR. SAMET: Thank you.

Dorothy?

DR. HATSUKAMI: Actually, I have a question for Dr. Curtin. Thank you so much for the extensive analysis you did on some of these surveys. But I have a question on whether you did another type of analysis, which is to take a look at current to former smoker ratio among those who are menthol versus non-menthol smokers, even within race.

DR. CURTIN: We did not. One of the surveys, and I believe it's the NHIS, we report a lot of the data for former smokers, as well, and it's in the manuscripts. I didn't talk about it today, because it's not that different from current smokers.

We were intrigued by the approach used by Gunderson, looking at former and current smokers to address some of these issues. We didn't start this work until the beginning of the year. We

wanted to get it into a position where we could understand the strengths and weaknesses of the analyses and the surveys.

We're attempting now to go back and look at other factors. I think that's an excellent idea. We're also embarking on the multiyear analysis, which I alluded to, as well.

So we weren't doing this work prior to the beginning of the year. We're just starting now.

This is where we are at this point. We do recognize that you could answer some questions looking at former and current smokers.

DR. SAMET: Jack?

DR. HENNINGFIELD: I have a couple of questions for each of the speakers. I have so many questions, and I think others will, too, that I think it may be in the interest of the speakers and in fairness to the process and them, to add a little bit of time to this. Let me just start with a couple, but they presented so many things that are at odds with my understanding of the same

literature, that I think we need to clarify some of these things. So very quickly, I'll just ask a couple to begin with, just clarifying details.

DR. SAMET: We just want to make sure, in our roughly 5 to 10 minutes left, we have time to get to the rest of the table.

DR. HENNINGFIELD: Then I'll just ask one or two to begin with.

Dr. Curtin, in the Moolchan and other studies, where you discounted their conclusions about dependence level, because you seemed to more heavily weight cigarettes per day, can you tell us the difference in number of cigarettes per day that they were seeing? You didn't mention the actual number of cigarettes per day difference.

DR. CURTIN: Okay. It was not my intent to discount Moolchan and Collins.

DR. HENNINGFIELD: And other studies.

DR. CURTIN: In fact, I raised those as studies that weren't discussed last time. So those weren't discussed last time. What I was trying to do is give a full accounting of the

literature.

So I raised studies that actually suggested that menthol cigarette use was associated with increased dependence. So we weren't only showing one side, I wanted to be complete.

What I did is reported that study. As they suggested, two of the four questions suggested greater dependence, two didn't. There was not an overall dependency score. I didn't assess whether that was a good or bad study. I just put it into context.

DR. HENNINGFIELD: Okay. My question was the difference in the number of cigarettes per day, because without -- in a couple of studies and in one of your slides, you mentioned cigarettes per day as a measure of dependence.

Can you tell us what the difference in cigarettes per day was?

DR. CURTIN: In that one particular study?

DR. HENNINGFIELD: Yes, and the others,

as well.

DR. CURTIN: No. No, I can't. There's probably 50 or 60 studies that were reviewed and referenced in this discussion. Now, we have provided detailed information in both our submissions of March 22nd and June 14th, I believe, where we've gone into these papers in great depth and tried to carefully and thoughtfully analyze the data and present it in a way that we think is fair.

But just picking one study out of those 50 and asking if I remember exactly how many cigarettes per day, no, I don't.

DR. HENNINGFIELD: Okay. Then a clarification that I'll make is that when you're talking about difference in cigarettes per day, and in some of these studies -- I'm familiar with them -- the difference is a few cigarettes per day.

In any scoring system, like the Fagerstrom or the heavy smoking index, the difference from 11 until 20 doesn't change the

score. So in other words, the difference in a couple of cigarettes per day is basically irrelevant.

DR. CURTIN: So we presented data from the national survey suggesting fewer cigarettes per day overall for menthol versus non-menthol cigarettes. We would argue that 2.5 to 3 cigarettes per day taken over a lifetime would be a significant reduction in cigarettes per day.

DR. HENNINGFIELD: When you say fewer, maybe you can come back to us and clarify what the numerical difference is. And if you're talking about dependence, as you did in your slide in your presentation, that's an important consideration.

Can I just have a quick question of the others? And I do have more on this, but I'll come back.

Dr. Hunter, this was touched on a little bit by Dr. Benowitz, but one of the, I think, great findings in African-American youth is lower overall rates of smoking and other drug abuse.

What's disturbing, as Dr. Benowitz

mentioned, is the apparently higher rate of conversion to dependence in adulthood, and that's really important to figure out.

Is that a cultural variable? Is it marketing? Is it menthol? And I think that's really important for us to figure out. Can you comment on that conversion? Because, Dr. Hunter, you focused on the youth difference, but not the adult difference or the fact that the adults tend to converge; that African-Americans tend to come up to Caucasians and, in some studies, be at higher rates.

MS. HUNTER: I don't know that I understand what your question is. And for the purposes of my presentation, I focused on youth and initiation. So I don't know that I can answer your question.

DR. HENNINGFIELD: So the apparently higher rate of convergence from the fact that they're a lower rate as youth, African-Americans compared to Caucasians, are then similar in adulthood, do you have any understanding of want

to comment on how that happens?

Because, remember, about 70 percent of those were initiating on menthol, and this is really important to try to figure out how we -- because if you just look at kids and stop at age 18, it looks like we're on the right path with African-American youth. And you look at about five or six years later and the story doesn't look so good. That's part of the reason we're here.

MS. HUNTER: Again, as we look at the information, we do see that African-American kids report smoking menthol at a higher rate of use than their white counterparts. But when you compare youth use of menthol to adults, it's actually a lower rate of menthol use than adult African-American use of menthol.

DR. HENNINGFIELD: By the way, you also referred to the 1994 Surgeon General's report, and I think others have, maybe yesterday. We were just starting to look at youth then. Menthol was hardly on the radar screen. The tobacco industry documents weren't out.

So I think the fact that a 15-year-old report didn't find this problem isn't very reassuring to us. Last --

DR. SAMET: Actually, Jack, let me move us down the table.

Patricia?

DR. NEZ HENDERSON: This is for Dr. True, on your graph on menthol market share.

DR. TRUE: Yes?

DR. NEZ HENDERSON: Do you agree that more than 70 to 80 percent of African-American smokers smoke menthol cigarettes?

DR. TRUE: Yes.

DR. NEZ HENDERSON: According to this graph that you just showed -- actually, the one before that one, or you can do this one, too. According to the U.S. Census, more than -- what is it -- 73 percent of African-Americans live in the east and the southern states.

Would you agree that 16 of the 20 states have the highest -- 20 of the 16 states who have the -- going from District of Columbia all the way

down to, I believe, Florida, are located in the south and east states, which is where 73 percent of African-Americans live.

DR. TRUE: That would appear to be consistent.

DR. NEZ HENDERSON: Thank you very much.

DR. SAMET: Greg?

DR. CONNOLLY: Dr. Curtin, could I ask you a question?

I thought it was my turn to ask a question. Yes. Dr. Curtin, please. Could you refer to slide 6, please?

If I look at slide 6, it indicates to me that menthol -- I appreciate your presentation. It's provided me with an enormous amount of knowledge -- that it appears to be there's a higher level of experimentation with menthol among younger age groups than the older age groups, even though this is a cohort study, this is not a longitudinal study.

Did I interpret that correctly?

DR. CURTIN: I think there's a higher

level of experimentation with adolescents, regardless of cigarette type.

DR. CONNOLLY: Okay. Well, let's talk about brands. In that 12 through 17-year age group, have you looked at the brands?

DR. CURTIN: The NSDUH data do collect brand information.

DR. CONNOLLY: Okay.

DR. CURTIN: It was not reviewed by the --

DR. CONNOLLY: Okay.

DR. CURTIN: Excuse me; if I could finish. It was not analyzed in the presentation you hard in March and it was not analyzed by us for a reason. Sub-branding makes t difficult.

So if you take a product like Marlboro, which has a significant menthol and non-menthol, and it is one of the major brands, then looking at branding doesn't help you, because you don't know, if they say Marlboro, if it is a menthol or non-menthol.

We were trying to work through that, but

people have added difficulty working through that.

DR. CONNOLLY: Okay. I don't want to take a lot of time here. But let's exclude Marlboro because of your issue. But just take a dedicated menthol brand. Kool is menthol and Newport is menthol.

Have you looked at the data of 12 through 17-year-olds on Newport and Kool?

DR. CURTIN: We have not yet.

DR. CONNOLLY: Okay. Excuse me.

DR. CURTIN: Again, we are attempting to look at all the data completely. So from a scientific standpoint, it doesn't make sense to take out the number one brand possibly or at least in the top three for adolescent smokers and just exclude it. I think that may be part of the reason why some of these papers have been critically evaluated, because of some of those decisions.

DR. CONNOLLY: All right. But if you look at the SAMHSA data for 2008, it would appear that the vast majority of those 12 through 17-

year-olds are smoking Newport.

Could you go to slide 18?

DR. CURTIN: I'm sorry. Are you asking me if that's true or not?

DR. CONNOLLY: No. I'm just reporting from the SAMHSA data.

DR. CURTIN: We don't have that information.

DR. CONNOLLY: Okay. Thank you. Well, I think science is important to this committee to look at in making decisions.

Could you go to slide 18, please?

Okay. Now, in slide 18, I'm just looking at the percent numbers and if I'm getting this right, it appears that 12 to 15 percent, in the NSDUH data, are smoking menthol in the past month. Am I correct?

DR. CURTIN: This is not brand-specific.

DR. CONNOLLY: No. I'm not talking about brand. I'm just talking about the overall menthol use.

DR. CURTIN: Okay. This graph does not

address overall menthol use. This graph addresses past month cigarette use.

DR. CONNOLLY: The top chart, what is the top chart?

DR. CURTIN: The top chart addresses male and female past month cigarette use. The first bullet and the second bullet are a lead-in into what we were just talking about on the previous slide.

The next bullet says that the NSDUH data provides information on past month cigarette use and past year cigarette initiation. Those are what's summarized to the left. So that's past month cigarette use, which is located on the Y-axis for the top graph, and past year cigarette initiation, which is clearly denoted on the Y-axis for the bottom graph.

These graphs have nothing to do with menthol cigarettes. They're overall past month cigarette use and overall smoking initiation, and these data are taken straight off the government Website. We didn't do any analysis with these

data.

DR. CONNOLLY: Okay. But if we go back to that earlier slide, we did see, at least in terms of initiation, higher rates among youth. Thank you.

Next, Dr. True?

DR. CURTIN: I'm sorry. But we didn't show any data that shows increased initiation among youth for menthol smokers.

DR. CONNOLLY: You showed data on a cross-sectional study from the SAMHSA dataset that suggested higher rates of initiation --

DR. CURTIN: No, we did not.

DR. CONNOLLY: -- among 12 through 17-year-olds.

DR. SAMET: Is there a clarifying question on the graph?

DR. CURTIN: If you're asking for a clarifying -- if you're asking us what we showed, the NSDUH, I said, may have been interpreted as suggesting increased initiation. What I said in the graph was that those datasets do not provide

information on initiating cigarette.

What the two surveys show or provide for is past month cigarette use or current cigarette use. Neither survey provides data on what cigarette was initiated with an adolescent. We don't know if it's menthol or non-menthol. If they initiate --

DR. CONNOLLY: You've clarified enough. Thank you.

DR. CURTIN: Well, apparently not.

DR. CONNOLLY: Dr. True?

DR. SAMET: Greg, how many --

DR. CONNOLLY: One question and I'm done, John.

DR. SAMET: One more question, okay.

DR. CONNOLLY: And I think these are important.

Can we go to chart number 8?

What is the scientific reason that the level of menthol in Newport is about half that of Kool?

DR. TRUE: I explained in great detail

yesterday the process with which we decide the level of menthol to put in Newport.

DR. CONNOLLY: But is there a scientific reason for that?

DR. TRUE: Taste. The balance of tobacco taste --

DR. CONNOLLY: Thank you.

DR. TRUE: -- and menthol.

DR. CONNOLLY: Thank you. Okay. The second question is what is the scientific basis for the high use of menthol among 12 through 12-year-old adolescents?

DR. TRUE: I don't have a --

DR. CONNOLLY: Thank you.

DR. TRUE: -- scientific reason why.

DR. CONNOLLY: Thank you. I'm done.

DR. SAMET: Thank you.

Corinne?

DR. HUSTEN: Thank you. I greatly appreciated the extensive analyses that were done in the background papers. I just wanted to ask one thing from those analyses.

It appeared, to me at least, that some of them looked at menthol use overall versus non-menthol, which, again, there is the confounding of race and cigarettes per day. Others seemed to look at analyses by race, not breaking it down by menthol or non-menthol.

So I'd just ask, in all analyses that are submitted, if the independent effects of menthol could be looked at with adjustment. And then my second request would be, also, to be very clear about the question used and the age asked across the various surveys, because, for example, some of the surveys ask adults 30 to 35 at what age they initiated smoking, which is a useful measure, but it's measuring initiation 15 years ago.

So I'm not sure a comparison with studies that are asking kids today what age they started -- so I would just ask that everything be very clear about what was the question, age asked, so that as we're looking at it, we can be very sure of what we're looking at.

So just a comment. Thanks.

DR. CURTIN: Let me try and address that. I believe for every analysis we did, there is unadjusted data, there are data that are stratified by gender, race/ethnicity, and a consistent breakdown of age, which is heavily weighted towards younger age, and it's consistent across all the datasets you have in front of you for all surveys.

Whether we looked at prevalence or we looked at initiation age or dependence or cessation attempts, we looked at the data consistently across all four surveys using the same metrics that we could. I think there's a slight change for NSDUH, because some of it's categorized data.

But if you look in those papers, they're structured a little differently because we want to submit them to a journal that makes you embed them into the text. But there are unadjusted, stratified, and regression model data for everything. There should be nothing we omitted, and I don't think there is anything omitted.

In terms of defining --

DR. HUSTEN: Okay. That's all at this time.

DR. CURTIN: -- current menthol use, that's not anything we do. I mean, we're taking all this data from the national surveys. So the national surveys -- and how they define menthol use.

DR. HUSTEN: No, no, no. I appreciate that. I was just saying if all the analyses could just be very clear about the question that was used across the different surveys, so that as we're looking at it, we can understand it.

DR. CURTIN: Sure. And what we've attempted to do, and if we were deficient, my apologies, but what we've attempted to do, since we're making some of these arguments, is to clearly define which surveys base it on usual brand and which surveys do not, which was the NSDUH, as well as the group setting information, and we've tried to lay that out all in the manuscript.

We'd be happy to provide additional information, if it would be of assistance. It's my understanding that FDA will be doing some of this analysis, and, as I said on my last slide, I think proper and consistent identification of current smokers and cigarette type are critical to getting reliable results.

DR. SAMET: David, questions?

Let me ask, are there follow-up questions that anyone would like to ask? We're thinking about finishing our discussion of this before the break we have not yet had.

Jack, one question.

DR. HENNINGFIELD: Dr. Curtin, we touched on this a little bit, but you talk about lower smoking intensity in a number of contexts. And can you just define what you mean by that? Because when it's taken in the abstract, it can be meaningless, if all you mean is a few cigarettes per day.

DR. CURTIN: When we talk about smoking intensity, we're specifically talking about

cigarettes per day. I think some of the smoking topography differences have been addressed in earlier presentations. We are only talking about cigarettes per day.

DR. HENNINGFIELD: And how much of a difference in the cigarettes per day do you believe is meaningful from the perspective of dependence, which you referred to in one of your conclusion slides and the opening, or from a health perspective?

DR. CURTIN: I don't know if that's known exactly what kind of reduction in cigarettes per day would lead to a more favorable outcome. What we're doing is reporting that there are reductions in cigarettes per day.

Part of this review was to look to see if there were any adverse effects associated with menthol smoking. And so we don't get lost in the fog here, we're not reporting increases or no differences. We're reporting reductions. So whether that reduction is three or 10, it was not an increase and it wasn't different. It was

statistically lower. Whether it's three or 10, it wasn't an adverse finding for population effects, both on initiation age, cigarettes per day, and attempted quitting.

DR. HENNINGFIELD: When we're talking about cigarettes per day, I think it will be important to put what the number is, because for dependence, that is important. And, again, as I mentioned, from a dependence perspective, from 11 to 20, there is no difference.

DR. CURTIN: And to be fair, in the manuscripts we provided, we didn't provide data as difference only. We provided the average number of cigarettes per day and the 95 percent confidence interval for all the demographic groups, and then the difference in the different columns.

So we have provided a full accounting of all the data and this is government data, which could be confirmed or recalculated by anybody.

DR. HENNINGFIELD: I come to different conclusions from some of those same studies.

That's why I want to try to understand your conclusion. I have several more, but --

DR. SAMET: I think we need to move on.

Neal?

DR. BENOWITZ: Dr. Curtin, I'm just going to follow-up on Jack's issue, because I think this is an important thing to get straight.

It's well known that cigarettes per day are not very good markers of intake of tobacco smoke, and Dr. Sarkar presented yesterday data with the biomarkers, which are a much better indicator, showing that even, say, the African-Americans smoked 1.5 or 2 fewer cigarettes per day, but their intake of nicotine, based on nicotine equivalence, wasn't the same in menthol versus non-menthol, and cotinine was even higher in menthol.

To me, what this means is that menthol cigarette smoking is associated with greater inhalation per cigarette, and, therefore, even if you're smoking two fewer per day, if your biomarkers are the same, your exposure is no

different.

So I don't think the relationship between menthol and cigarettes per day has any weight with respect to addiction or risk.

DR. CURTIN: We've addressed that issue head-on in the manuscripts. I didn't address it in the talk. There are a number of studies that have suggested that this compensation you're talking about does not occur, including a study recently in 2006 by O'Connor that showed no compensation for fewer cigarettes per day on a population level.

DR. BENOWITZ: No. Now, I'm not talking about compensation. I'm talking about you cited or someone cited that the Sarkar data was really, really important because it was the largest biomarker study. This study, which looked at nicotine equivalence and looked at cotinine -- this is not about compensation for fewer cigarettes per day. It's still got menthol versus non-menthol, and there are biological reasons why menthol could be associated with greater

inhalation per puff.

The Sarkar data suggests that, in fact, that's the case, because cigarettes were fewer, but the nicotine equivalence and cotinine levels were the same. So I think when we're talking about menthol versus non-menthol, it's not the same as compensation.

I think, for this, we can't assume that fewer cigarettes per day mean less exposure.

DR. CURTIN: Well, I appreciate the point. And I think the TES study stands for itself. We can't look at those type issues from national survey data. So what we are attempting to do is report what we could look at. So taking a metric that was in this total exposure survey and applying it to what we're doing, where we're getting government numbers that don't address the things you're talking about, what we're able to do is report cigarettes per day.

That's where we started. It doesn't mean we're necessarily done there. That's just where we started. But we can't even venture into any of

the things really that the really nice TES looked at. That data is just not collected.

DR. SAMET: Dr. Sarkar, you have a brief comment?

DR. SARKAR: Dr. Benowitz, you pointed out that when we showed the data on the nicotine and the serum cotinine, that there is this apparent increase in the menthol in African-American smokers, despite them smoking about 1.5 to 2 fewer cigarettes than the non-menthol African-American smokers.

But I think we also need to remember that if you look at the average tar yield, the tar yield of the menthol smokers was about 12 compared to the non-menthol smokers, which was about 6.

Then as far as the puffing parameters, I didn't show the data, but we think that the exposure, like nicotine equivalence, the daily excretion of nicotine equivalence is kid of a composite and integrates all these different behaviors. And there was no statistically significant difference after you adjust for the

CPT, as well as for the tar yield.

In absolute terms, when you look at the raw data, the nicotine equivalence was higher, but it was not statistically significant, even in the univariate comparison, as well as in an ANCOVA model.

I think it's far complex, because you've got other factors that could be playing a role, like, as I said, the tar yield was much higher.

DR. SAMET: Thank you. I think we have two more questions.

DR. BACKINGER: I'm going to pass, in the interest of time.

DR. SAMET: Patricia?

DR. NEZ HENDERSON: This question is for Ms. Hunter. We have been charged to look at the impact of use of menthol in cigarettes on the public health. Yesterday, I gave a definition of public health. Just to refresh your memory, it's the science and art of preventing disease, prolonging life, and promoting health.

Do you believe that menthol cigarettes is

promoting health among African-Americans? So if menthol is preventing disease, prolonging life, and promoting health, this is the language that we have to work with. So that's my question to you.

MS. HUNTER: And my response to that is we heard yesterday, my colleague, Dr. Lewis, there are no safe cigarettes. Menthol and non-menthol are no different.

As I shared in my comments, kids should not smoke menthol or non-menthol cigarettes. What I hear you asking is a policy question. I'm not prepared to answer that. But what I would offer you is kids shouldn't smoke any cigarettes, menthol or non-menthol.

DR. SAMET: I'm going to take the chair's prerogative to ask an answerable question.

[Laughter.]

DR. SAMET: This is actually for Dr. Curtin. I'm just curious as to your choice of journal for submitting these papers. I recognize this was an online journal. It's a little bit outside the usual venue for publications on

tobacco.

Why did you select it?

DR. CURTIN: Actually, an online journal was my decision, and we haven't made a total decision yet. But we had been contacted by that journal. Being an online journal gave us the latitude to present a lot of data and not have to cut down all the tables, and we were informed that they were going to be running a special issue on tobacco smoking and public health. So it seemed opportune to at least look at that journal.

DR. SAMET: I was just curious. I recognize the dilemma of trying to publish large papers with lots of tables. It's not necessarily a journal that will reach broadly to those who work in tobacco control nor necessarily one that may secure you the tightest peer review. But I think it was just a matter of curiosity on my part.

DR. CURTIN: The two considerations were that they were running a special issue and apparently have run special issues before, and we

thought that all the data that we had to provide, 32 tables, would be -- that would be a limiting factor on a non-online journal.

DR. SAMET: Great, thanks.

See, I did ask an answerable question.

Now, we are going to take a 15-minute break. Let me remind the committee members, no discussion of the meeting topic during the break amongst yourselves or with any member of the audience. Back at 10:40. Thanks.

(Whereupon, a recess was taken.)

DR. SAMET: We are moving on to the open public hearing, and this is what we were going to do, I think, before lunch.

Both the Food and Drug Administration and the public believe in a transparent process for information-gathering and decision-making. To ensure such transparency at the open public hearing session of the advisory committee meeting, FDA believes that it is important to understand the context of an individual's presentation.

For this reason, FDA encourages you, the

open public hearing speaker, at the beginning of your written or oral statement, to advise the committee of any financial relationship that you may have with the sponsor and its product and, if known, its direct competitors.

For example, this financial information may include the sponsor's payment of your travel, lodging or other expenses in connection with your attendance at the meeting.

Likewise, FDA encourages you, at the beginning of your statement, to advise the committee if you do not have any such financial relationships. If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking.

The FDA and this committee place great importance in the open public hearing process. The insights and comments provided can help the agency and this committee in their consideration of the issues before them.

That said, in many instances and for many

topics, there will be a variety of opinions. One of our goals today is for this open public hearing to be conducted in a fair and open way, where every participant is listened to carefully and treated with dignity, courtesy and respect. Therefore, speak only when recognized by the chair. Thank you for your cooperation.

Now, just to the committee, so you know, we have four speakers who have signed up in advance and they each have 10 minutes for their presentation. We have an additional four speakers who have signed up. They have each been allocated three minutes.

So to get this public session done and to move through it expeditiously, if there are, I think, important clarifying questions, we can ask a few. I think otherwise, we need to move through so that we hear from as many of the public as possible.

Speakers, we will ask you to terminate your presentation at the time you have completed your allocated time. And for those speaking for

three minutes, there will be a buzzer and when you hear it, please end your sentence that you're on at that particular point.

So with that, we'll move to our first public speaker in this session, William Robinson, from the National African-American Tobacco Prevention Network. Please.

MR. ROBINSON: Good morning. And I want to thank the committee for allowing me a few moments to speak this morning. I am, for those of you who don't know, William Robinson, the executive director of the National African-American Tobacco Prevention Network. And I have no financial relationship with the sponsors of this event.

As I come before you this morning, I must say that I was having some conflict about if I should present on behalf of our organization or personally, as I didn't want and wouldn't want my organization to be responsible for comments that I might make for an issue that I'm very, very passionate about.

Our organization has a single mission; that is, to serve as a national organization dedicated to facilitating the development and implementation of comprehensive and community competent tobacco control programs to benefit communities and people of African descent. That's all we do.

We have been doing so for 10 years and now just celebrated our first decade of service to communities and individuals across this nation.

In my testimony today, I wanted to take a different approach. I want to bring you something that the committee, I think, has been lacking in both meetings thus far. So I'm not going to present any statistics. I'm not going to show you any charts. I'm not going to quote any articles. And I'm going to tell you a -- I'm not going to tell you how many times, also, that I've engaged the media since May of 2008, although I did talk to CNN on Wednesday and KNX out of Los Angeles on yesterday about this very meeting.

What I want to do is apologize first. I

want to apologize for not getting my comments to you via e-mail, because I was on a much overdue vacation last week. I really wanted to get a few slides to you, because they would have served for the foundation of my comments today and let you know why I've been doing what I've been doing for so long.

What I wanted to share with you were four pictures, a copy of a medical document, a quote, and pose a question to you that I haven't been able to get an answer for for more than two years now.

If I might, I just want to take a few minutes to share a story with you. The story for me begins in October of 1955, the month and the year of my birth, but began for the subject of my story on February 23rd, 1933.

In the midst of a looming depression, a baby boy was born top Elijah and Lucy Robinson in Camden, South Carolina, William Robinson, one of 11 children that they would have.

I am told that from birth, this child

exuded strength, confidence, and an abundance of common sense that was eventually supplemented by only six years of formal education. The young man emulated everything that his father did, including working in the corn, cotton and tobacco fields of rural South Carolina, until he was old enough to convince people that he could drive anything that had wheels. And once he could, this young man began driving trucks, tractors and vehicles that widened his world beyond the small town that he grew up in, always sending part of his earnings back to support his family and his siblings.

From as early as I could remember, my dad watched his father maneuver a substance from a Prince Albert tin can and drop it between strips of white paper that he kept folded in waxed paper in one of his back pockets. He would roll that thing so perfectly and smoke it in a way that my father thought, "What kind of pleasure," it was more than humanly possible.

This always made my dad, his siblings and other youngsters in the community curious and they

used to pick up the unfiltered butts from the ground as they walked to school and made their own versions of the same.

At 9 years old, my dad had tasted tobacco for the first time. After he began working for wages at age 13, he was able to purchase his own and settled on Blue Bugler, a brand that was advertised at that time to represent price and dependability.

Our organization just recently located a can of this same tobacco and it now says "Solid values that remain today, since 1932."

If we fast-forward to 1955, I was born on Long Island, New York, in a town named Manhasset. I spent a good portion of my first two years back in Camden at my paternal grandmother's home, as my parents sought housing as a part of the great migration of African-Americans from the deep south, seeking better economic and employment opportunities.

My paternal grandfather, I'll never forget, Paris Brevard, Jr. (ph), always smoked a

corncob pipe. In early 1959, our family was selected to occupy one of the units in a newly-built public housing community and from 1959 until I graduated high school in 1973, my siblings, my mom, and I inhaled the secondary smoke from my father's three-pack-a-day consumption of cigarettes and occasional cigar, including his propensity to light the next smoke from the one that was nearly finished, a chain smoker in the truest sense, all mentholated, after a short experience with Pall Malls and unfiltered non-mentholated Camels.

My dad, who had a very successful landscaping and snow removal business, continued to smoke this way until the summer of 1981. During the summer of 1981, when my brother and I were managing his landscaping business, my father was painting a couple of houses in Kings Point, which is a section of Great Neck, New York.

One Wednesday evening, after what was otherwise a normal day, we returned the landscaping truck to my parents' house and noticed

hr were more cars around than usual. When we walked into the house, mom was crying uncontrollably. We were met with the kind of avoiding glances that always indicates serious trouble, and we learned that earlier that day, my dad had fallen backwards off his ladder off of two stories. He was completely paralyzed, unconscious, and had been flown to a New York City hospital by helicopter, with his life in the balance.

As a young man who had just reentered college in the previous semester and pursuing my undergraduate and focused on a graduate degree, I was presented with questions that I wasn't prepared for. Should I continue my studies? Do I run the business to ensure that mom won't lose the house? How bad is dad? Will he live? What will his family do without him?

Four days later, I was in the hospital when my dad first moved his head and regained consciousness. The very first thing he asked for was a cigarette. He didn't want to know how he was or how I was. He didn't want anything to eat

or drink. He asked for a cigarette.

That afternoon, I became a tobacco control advocate, because I wanted to know what was in this foreign object that had the man that I admired most in the world wake up from near death and that was his first request.

I informed the doctors of my request and they immediately came in to speak with my father and explained to him how continuing to smoke would jeopardize his recovery. After the session with the doctors, I had the most difficult conversation I've ever had with my dad and told him that he had to give up smoking for the family's sake.

Thankfully, he did that day, but not without repeated attempts, serious difficulty, a couple of short relapses, and hundreds of Tootsie Roll pops.

My dad currently lives in his home independently in Camden, South Carolina, just celebrated his 77th birthday, and is now becoming an expert in his motorized wheelchair as he goes out to water his garden a couple times a week. He

also can't stand anybody who smokes anymore and makes people air themselves out before they enter his home.

I wanted to provide this story to put a human face on this issue at hand. My dad is not well enough to travel anymore and he would be with me here today personally telling you this story if he could.

The medical document that I referenced earlier is an EKG of my heartbeat, and it's anything but. If you didn't know, my EKG reads like I'm having a heart attack every few minutes, and this is from a person who was a three-sport athlete, made the Division I basketball team, and still very physically active.

So where did this all come from? Where did this irregular heartbeat come from? It's been confirmed that it's prolonged exposure to tobacco smoke.

Now, you know what I've been doing with my life for the last 29 years and why I do it. And in those 29 years, I've learned a couple of

things, and that's the natural properties of menthol don't change, whether it's in gum, candy, sports creams, shampoos, or tobacco products. It soothes and cools anything that it's added to.

But when I began in tobacco control, a little more than 55 percent of African-American smokers smoked mentholated products, and it's now 83 percent; that the evidence is growing about the role of menthol and addiction, difficulty in quitting, and cessation.

[Microphone times out.]

DR. SAMET: Thank you. I think if you could end your presentation, please. It's a compelling story and a long one, I'm afraid. But thank you.

Committee, questions, comments at all?

[No response.]

DR. SAMET: Okay. Thank you.

Then we'll move to our next presentation by Jim Tozzi, the Center for Regulatory Effectiveness.

MR. TOZZI: Good morning. I am Jim

Tozzi, with the Center for Regulatory Effectiveness. Mr. Chairman, distinguished members of the committee, I appreciate the opportunity to make a statement. I also appreciate having 10 minutes, which I won't take this time, compared to the three I had last time.

I would want to make two recommendations to you all, and they're not all that complex. First, I would recommend that the committee spend some time on complying with Section 907(b)(2) of the statute. And as you may recall, or you may not recall, and I haven't heard it discussed in your proceedings, that portion of the statute, which is part of your organic statute establishing this committee, states, in part, "The Secretary, in considering a tobacco product standard, shall" -- "shall" is not permissive, not "may" -- "consider information concerning the countervailing effects of a tobacco product standard on the health," and underlined, "of non-tobacco users, such as the creation of a significant demand for contraband."

That is a direct requirement of the statute for the committee. I haven't heard that discussed much, and I encourage you to really look at that.

Before I proceed, since I do have 10 minutes, I'll make a statement on the financial disclosure. Our center gets contributions from every sector of the American industry, including tobacco. We do not represent anyone in our watchdog role. All our work products are produced by us, they're being produced this very minute, and none of them are reviewed by any of our sponsors whatsoever.

Now, back to this issue of contraband. Why it is significant is because people are going to ask, and it's already on the Web, a number of people were asking, would a lack of the availability of menthol cigarettes give rise to a rampant black market in off-brand menthol cigarettes, with the resultant violence that has happened in a number of areas?

Those of you that are students of this

area will look at what happened in prohibition, look at what's happened in marijuana, which our center is very actively involved in, at least in the legalization of medical marijuana. And questions are going to be asked. To what extent, on the non-tobacco users, which you're health professionals, but these are these are the non-tobacco part, will this have an impact on them?

Now, we do work around the world and, let me tell you, those of you that follow what's happening in Mexico, the carnage that's happening in Mexico, part of it is driven by contraband products in this country that has financed, in large part, the operations of hostile operations against a lot of citizens of Mexico. I'm not yet suggesting in any way that this is of that magnitude. It's something to be considered.

Now, what do we recommend? CRE is involved in the activities of nearly federal agency or at least regulatory agency and has data documenting the creation of black markets. Consequently, CRE will be providing an in-depth

analysis of this issue to both the FDA and to TPSAC.

Now, the way we communicate with federal agencies is a mechanism that we developed called interactive public docket. All of our information that CRE ever develops is on an interactive public docket. There is no ex parte contacts. It's all available for the public to comment.

This document that we'll be presenting to you will be sent to you simultaneously through the docket, and we request public comments.

Now, another point in this regard. The incorporation of contraband considerations into this proceeding is a risk management, not a risk assessment decision. Notwithstanding the very impressive credentials outlined by Dr. Sharfstein this morning, the credentials of this committee are very heavily oriented towards a risk assessment phase of this operation, not the risk management side.

There's not a whole lot of experience on the panel of those that held government positions

that have to make binding -- binding -- risk management decisions on the population.

Now, this is not to suggest that this panel, with your extensive background in public health, can't make an informed decision, but we at CRE would hope that you would consider having a session and developing a protocol for the manner in which the contraband consideration can be incorporated into the calculus of your recommendation on menthol.

My second recommendation, which I mentioned before, which I don't think it will be new to you, having been either in or out of the bureaucracy for five decades, I understand the power of the pen and I understand the power of that person who writes the first draft of any document.

As I said before, I hope that the ex parte rules of this committee do not preclude in any way that the first draft of the committee report be prepared by the informed members of the committee and not by the FDA.

I don't make this recommendation in an insular setting. I've participated as a member of advisory committees for a number of decades, and I know well the impact of who prepares the first draft, and I would hope you'd give serious consideration to the first draft being prepared by the committee.

Finally, I would like to compliment the career staff at FDA for really holding this particular meeting, keeping the stakeholders well versed by publications on the Website, and making it very clear to some older people that testify that you've got to ask for your comments in advance and you'll get the full 10 minutes.

I'll relinquish the balance of my time to the committee. Thank you.

DR. SAMET: Thank you for your comments.

Questions, Jack?

I think we do have a question for you.

DR. HENNINGFIELD: The comment about the distinction between risk assessment and risk management is important, and you're undoubtedly

aware that the FDA, since about 2000, is increasingly risk management focused.

But I guess what I didn't understand is your recommendation that menthol in cigarettes should not be regulated or banned by FDA because of the concerns or that if it does ban menthol, that it should attend to issues like contraband and how it does it to manage those risks.

I guess I wasn't clear.

MR. TOZZI: The point is this. It's a process concern that the statute requires that this committee look at contraband, and contraband is a data point -- it will be a risk assessment, per se, in one way, of really how bad that risk is.

But then the committee is going to have risk assessment data on direct health effects. It's going to have risk assessment on what I think is a very big, important issue, cessation and initiation, and a risk assessment on a completely different kind of animal, which is contraband.

So I'm not suggesting how you all come

out. I'm just saying the incorporation by health professionals of non-health-related data, not that you can't make very informed decisions, but I think it needs a protocol that looks at how that balancing is going to take place, how it's going to be incorporated into the record.

We at CRE have not taken -- now, we have taken a position on one or two of the studies that we don't think meet the Data Quality Act, but we're not in a position to look at that entire record on the merits, at least yet.

DR. SAMET: Thank you.

I think we should move on to the next presentation. This is David Johnson from CITMA, C-I-T-M-A.

DR. JOHNSON: Good morning, Mr. Chairman, distinguished members of the committee. My name is David Johnson, and I'm here as a consultant representing the small tobacco manufacturers and providing you with their perspective around menthol and what their situation is and how it's significantly different than the situation that

exists for the major tobacco companies.

Menthol itself is a very simple product. It's something that's been used for an extensive period of time, and it's been used by the major tobacco companies significantly. The small companies, however, have been using it, as well, but they don't go into the process of manipulating the levels of menthol in their products.

They have a situation where they are small; they do not have a lot of resources; they don't do significant research; they don't have large science departments. Their ability to do some of this work is very, very restricted. And so what they do is they acquire their materials by benchmarking against competitive products in the marketplace that are produced by the major producers. They take that and, by taste, then produce products that they can use to enter the marketplace.

In general, these small companies do not market their products through mass media. Principally, they use point of sale advertising

that is designed to attract dealers, distributors, wholesalers, and maybe some adult consumers, but generally, it's very, very restricted.

They advertise in trade magazines. They don't do it in mass media and ways that would get to youth. And so their advertising is restricted. Youth appeal is typically not an issue with these products, as they tend to be off-brand products. They don't have the appeal, the brand appeal, that you tend to look for in many of the products that they will experiment with and use.

The products that they produce are sold primarily to older people who are price conscious and price sensitive. And so their products are purchased and produced in a separate manner. They buy tobacco typically and fabrication materials that are prepared by someone else and they basically assemble the product for entry into the marketplace.

So they have very little involvement in the actual processing of some of their products. What they end up with is a product that's very

similar to other products that are already in the marketplace. Not a lot of engineering goes into it, but a lot of quality goes into the actual production.

That's how they differ from the products that you have been talking about previously. The menthol is the same. The effects are the same. So if you have any questions, I'll be happy to answer them, but I believe that was the last slide in my presentation, which was just short, to describe to you what the position is for these small manufacturers who have a very different operation than the major tobacco manufacturers.

DR. SAMET: Thank you.

Greg?

DR. CONNOLLY: When you select the level of menthol, are you more likely to select a level that's similar to Newport or a level similar to Kool among your manufacturers?

DR. JOHNSON: This is a group that includes a very large number of producers, and so that's a very difficult question to answer and it

probably varies by the individual company.

You'll probably see some that are at one end and you may some at the other end. But in general, what you will find is that none of these producers produce a product that they market and market as a mentholated cigarette, in general.

DR. CONNOLLY: Would they agree to just one level?

DR. JOHNSON: I would have to discuss it with them. I'm here describing the process and the science. I couldn't make an agreement for them. But I will tell you that I'm sure that there is a range and when you say level, you probably are talking range anyway, because you're talking about a manufacturing process that's going to have inherent manufacturing variability.

You also are going to have a product that is going to be distributed, because of the physical properties of menthol over time, differently in the product. And so you'll get a different response as you age the product versus freshly prepared product. So you really do have

to talk about a range.

DR. SAMET: Mark?

DR. CLANTON: Dr. Johnson, do the small manufacturers, either collectively or individually, offer incentives, financial incentives at point of sale or discounts to those outlets to sell cigarettes?

DR. JOHNSON: My understanding -- and, once again, this is a very large group, and so I'm speaking for a very large group. But my understanding is that, in general, the pricing of non-mentholated and mentholated cigarettes with these companies is essentially the same and they don't have a tiered pricing structure.

Now, if you go out and you find one, I'm not saying that it doesn't exist. I'm not aware of it, because of the size of the group, but I don't think that they do that, in general.

DR. SAMET: Jack?

DR. HENNINGFIELD: You seemed to imply, and I just want to clarify it, that there's some distance between small manufacturers and the youth

market and the implication was that the larger companies -- they're the ones that start the youth market, then you reach adult smokers by price.

DR. JOHNSON: No. I'm not trying to imply anything about what any other company does. What I'm saying is that these small companies never target mass media or any advertisements to that segment of the population, and so they're not trying to attract that group. What someone else does, I can't say. But I can say that based on the interaction I've had with them, that that's not where their focus is. Their focus is on the older established menthol smoker who knows what they want and they go out and they buy a product.

DR. SAMET: Patricia? Okay.

Thank you for your comments.

DR. JOHNSON: Thank you.

DR. SAMET: Next, Rod Lew, Asian-Pacific Partners for Empowerment, Advocacy and Leadership, APPEAL.

MR. LEW: Good morning. My name is Rod Lew, and I'm the executive director of Asian-

Pacific Partners for Empowerment, Advocacy and Leadership, otherwise known as APPEAL. I would like to thank the committee for the opportunity to present, and I have no financial relationship with any of the sponsors.

In addition to being a national health justice organization for 15 years, APPEAL has also created a 600-organizational member national network that provides a critical voice for Asian-American, Native Hawaiian and Pacific Islander communities adversely impacted by tobacco.

We have heard many stories of how our communities are disproportionately impacted by tobacco, but unfortunately, not everyone has a voice to be able to tell their stories.

First of all, there is not a single Asian-American/Native Hawaiian/Pacific Islander community, or AANHPI community. Rather, Asian-Americans and Native Hawaiian/Pacific Islanders comprise more than 50 distinct ethnic groups living in the 50 United States and six U.S. associated Pacific Island jurisdictions.

In addition, the Office of Management and Budget considers the Native Hawaiian and Pacific Islander community as a distinct racial/ethnic category, which makes the issue of menthol particularly significant because of the high rates of menthol use among Native Hawaiians.

Tobacco is the single most preventable cause of death for AAs and NHPIs, who, combined, represent nearly 5 percent of the total U.S. population and are one of the fastest growing racial/ethnic populations in this country.

Asian-Americans and Native Hawaiians/Pacific Islanders, in the aggregate, have often been reported nationally as having one of the lowest rates of smoking prevalence. However, local studies have shown that males among certain Asian-American subgroups actually have some of the highest smoking prevalence in the United States; for example, a range of anywhere from 39 to 71 percent among Cambodian males, as indicated in the far left bar.

Tobacco use is also high among Pacific

Islanders, with the example of 42 percent smoking prevalence among Native Hawaiian males. And in 2004, Guam, one of the U.S. associated jurisdictions, with a predominantly Asian-American/Pacific Islander population, had the second highest adult cigarette smoking prevalence of all states and territories.

Data does not do justice to show the tremendous impact of tobacco on our communities, because either national data is not disaggregated by subgroup or data is not collected in the appropriate language, or sometimes not at all. And, frankly, as a result, more often than not, our Asian-American/Native Hawaiian/Pacific Islander communities get left out of the national discussions around tobacco-related issues.

Ironically, the tobacco industry has good data on our communities and have industry documents showing that they targeted the Asian-American/Native Hawaiian/Pacific Islander communities, because they are a very important group for the targeted marketing of their tobacco

products; one, because of the tremendous population growth; two, because of the great consumer potential they saw for our Asian-American/Native Hawaiian/Pacific Islander smokers, especially women; three, the potential partnering with many Asian-owned retail and convenience stores to increase their sales; and, also, the linkage between Asian immigrant communities in the United States and market expansion of tobacco products into Asia and the Pacific Basin.

The menthol issue is, sadly, no different. What I would like to share with you today are some of the limited data that we have on menthol for our communities.

Nearly 60 percent of all Hawaiian adult smokers smoke menthol cigarettes, as indicated in the second bar from the left. More than 50 percent of Asian-American youth smokers smoke menthol, a rate secondly to the African-American youth. And Hawaiian youth have increasing rates of menthol use for both middle and high schools.

Furthermore, the menthol campaigns

targeted at inner city youth are also affected and impacting our Asian-American/Pacific Islander youth, particularly those from low income communities, like the Cambodian, Vietnamese, and Laotian communities.

Rightly so, there is a great need to acknowledge and eliminate disparities of menthol use among African-American smokers. We should also add to that list other communities of color that are impacted by tobacco and menthol.

It's not just an issue of comparing the percentage point differences among the groups, but simply stated, menthol impacts all of our groups and communities. What we should be focusing on instead is the effect that menthol has in widening disparities among those groups already experiencing tobacco disparities.

So the concern is how are we defining harm in relation to menthol? If we use a narrow definition of harm of menthol, it's only focused on the biochemical impact, then we are missing a larger picture of harm. Menthol as a flavoring

makes it easier to smoke cigarettes. It's a starter product for youth and targets communities of color.

As Dr. Phil Gardiner states, "Harm is a social justice issue that magnifies the disparities on those populations that are most vulnerable."

If we imagine menthol as the icing or sprinkles on a donut, it adds flavor to a plain donut and makes it that much easier to swallow. Obviously, it is not intended to compare donuts with tobacco, because we know that nothing is as deadly as tobacco. But maybe this is also too simplified an illustration, but I wanted to show the relationship between menthol in tobacco and menthol as the icing that makes the poison of tobacco go down that much easier.

While additional research on menthol may still need to be done, we don't need more studies to tell us that menthol is harmful, just like the other 13 flavors that are already banned, and that it disproportionately impacts racial/ethnic

communities and widens the tobacco disparities.

The FDA should ban menthol to tobacco products now.

We recognize the success and value that tobacco financial policy has played around the tobacco issue, through tobacco tax or clean indoor air. We also must understand the importance of community-based approaches on tobacco control that are critical to eliminating tobacco disparities.

There needs to be more concerted efforts, supported with dedicated resources, to community-based organizations to reach out to those that are impacted by menthol.

A key acronym used for a comprehensive tobacco control framework at CDC and the World Health Organization is MPOWER. MPOWER represents the strategic comprehensive approach. I would add another letter, D, at the end, for defeating disparities, which would convert the MPOWER framework to an MPOWERD framework.

If we don't address disparities, and menthol is a prime example of a disparity in

social justice issue, we will not meet the Healthy People 2020 goals.

Only MPOWERD communities can prevent the continued uptake of menthol products among our youth; only MPOWERD communities can educate and expose the broader harms associated with menthol; and, only MPOWERD communities can raise the necessary public outcry that must be heard and listened to, even at the FDA.

So in conclusion, specific Native Hawaiian, Pacific Islander and Asian-American groups are greatly impacted by menthol. We must broaden the definition of harm for menthol as a social justice issue. We must ban menthol and we must build in resources to ensure that all of our communities of color are actively engaged in the implementation of the FDA legislation so that it can be properly enforced on all levels.

Only then can we truly realize MPOWERD communities and a truly MPOWERD nation. Thank you very much for your attention.

DR. SAMET: Thank you for our

presentation. John?

DR. LAUTERBACH: Sir, you mentioned various sensory properties of menthol which seem to be at odds with what my own personal experience is and that of others.

Do you have any sensory data, conducted under normal protocols, or sensory studies that would justify your assertions about menthol, where you've actually had smoke panel data run under controlled conditions to support your assertions about menthol?

MR. LEW: There was an entire conference dedicated to menthol and menthol impact, and we can get you some of those notes and references to those studies that have been done.

DR. SAMET: Continuing on. Ursula?

DR. BAUER: Thanks very much for your thoughtful comments. I wonder if it's your belief that if menthol had never existed as a flavoring in cigarette products, if we wouldn't have the same rates of smoking among these populations or if menthol were eliminated, these populations

wouldn't have the same rates of smoking.

Would they not smoke because menthol cigarettes are not available or would they not have initiated in the past had menthol not been available?

MR. LEW: Well, I think initiation is complex, but I think menthol plays a particular role in encouraging those who are vulnerable to take up smoking. I don't have the studies with me to demonstrate that. We certainly can get those references. And I think there still needs to be work done on particular populations, but I think it's key to look at those communities and populations that have high menthol use and how difficult it is for them to quit smoking.

DR. SAMET: Mark?

DR. CLANTON: Mr. Lew, thank you for your presentation. I spend a lot of time on Oahu for professional reasons and, also, visited Guam this year. There's a clear connection between what some Asian groups do in their home countries before coming into Hawaii; for example, in the

Philippines, very high persistent rates of menthol use among adults; also, on some areas in the Pacific Rim.

So culture has a connection with menthol use. What else is driving menthol cigarette use in the Islands? Is it marketing? Is it price? What's really going on at the street level?

MR. LEW: Well, I think part of it is availability, part of it is marketing. And I think it's difficult with our community, because our community is so diverse, that there isn't really good data to break it down for each particular group.

But as I mentioned, for some communities, like Southeast Asian communities, Vietnamese, Cambodian and Laotian, are very much affected by targeting in inner cities. So it doesn't necessarily have to feature faces from our communities, but it could be the hip-hop generation ads that are placed that also impact our communities that will encourage them to smoke.

The other piece around it is it builds

upon and it preys upon the income status and situation of where the communities are. So if it's a poor community that does not have access to resources, tobacco added with menthol will help to encourage those people to smoke.

DR. SAMET: Thank you.

How many others have brief questions? Jack?

DR. HENNINGFIELD: Could we put the MPOWERD slide back up? This is really useful and I'm just asking you for a quick opinion and then maybe something you might provide subsequently.

The opinion is how would you see a menthol ban that you seem to call for fit in that and what difference would it make? In other words, how would it work? I think we all know it's naive to think you just get rid of it and kids stop smoking.

So how would you fit it into public health?

Then what you may or may not be able to provide today is I think it would be really

valuable for the committee and for the FDA to have a better understanding of what's similar and different about the populations that you represent and the African-American experience. What can we learn? Is it exactly the same thing that's happening or is something different happening?

MR. LEW: I think there were three questions in there and I'll try to answer as much as I can. In terms of where a menthol ban would fit under there, I think it cross-cuts many of the different pieces. The reason I added the D for disparities is that many of the policy change which has been the focus of tobacco control has been very successful, and that's demonstrated by all of the MPOWER acronym.

But I think the other piece that we have to put on the front burner is that we can be successful with policy change, but until we integrate specifically disparity issues, and menthol being one of those issues, on the table as part of that framework, then we're hoping that things get trickled down through the other

mechanisms.

So I see that there may be opportunity to address a menthol ban in many of the other words of MPOWER, but the D, in particular, is something that puts it on the front burner, so to speak. And we can certainly offer some other information about what we have around how the similarities perhaps between the Asian-American, Native Hawaiian, Pacific Islander, and African-American communities, although that data is very limited.

DR. SAMET: Patricia?

DR. NEZ HENDERSON: Thank you, Mr. Lew, for your presentation. How many people live in Hawaii? Do you know the population size of Hawaii?

MR. LEW: I don't have that number right off.

DR. NEZ HENDERSON: Or just the percentage of Hawaiians, Native Hawaiians that live in Hawaii.

MR. LEW: I think it's about --

DR. SAMET: Mark?

DR. CLANTON: I think the population of Hawaii, the islands combined, is about 1 million, 1.1 million or so. Most of those are on Oahu. And I don't have the percentage, but percentage of Native Hawaiians is very small reflected against the total.

MR. LEW: Can I also just mention that there are also Native Hawaiians throughout the continental U.S.? In fact, that population is greater than the Native Hawaiian population in Hawaii.

DR. NEZ HENDERSON: The reason why I ask that is Dr. True presented this morning the menthol market share, and Hawaii is the second highest, about 65 percent. So I'm just kind of thinking out loud what that impact has on the high rates of smoking -- of menthol smokers among Native Hawaiians. Thank you.

DR. SAMET: Greg?

DR. CONNOLLY: Number one, thank you very much. I think that this committee needs constituencies for science. We have to make our

decisions based on science.

FDA traditionally looks at science in terms of safety and efficacy of clinical effects on individuals. So that approach is done fairly well within very controlled clinical trials.

Yet, this committee is charged with looking at population effects. So we're really trying to grapple with issues, I think, of community-based research. Now, a number of groups representing disparities groups have come forth and presented, but I would challenge you -- all of the groups represent disparity groups -- to do community-based research following standard accepted guideline and present it to this committee so that we can incorporate population-based science from communities across our nation and not make decisions solely based on whatever is generated within the traditional precepts of the FDA.

DR. SAMET: Greg, the question?

DR. CONNOLLY: It's a challenge rather than a question.

DR. SAMET: Dan?

DR. HECK: A quick question, kind of building on what Dr. Nez Henderson mentioned with regard to Dr. True's slide. I do notice, just visually, looking at that graphic, that Hawaii appears to enjoy a youth smoking rate -- a very low youth smoking rate, about half that of the national average, in the face of one of the highest menthol preferences generally.

I do appreciate and we discussed this morning the desirability of having ethnic-specific breakdowns of the youth smoking rate, which may be available in the statistics.

But in your view, does the fact that Hawaii appears to have about the second highest menthol preference among the 50 states, and yet one of the lowest youth smoking rates, does that dissociate, in your mind, the presence of menthol on the cigarette market from youth smoking initiation?

MR. LEW: Well, again, if I can just mention that the Native Hawaiian smoking

prevalence includes both those in Hawaii and the other states. I think we still need to tease out the distinction between what's happening in the Islands versus what's happening in the rest of the continental U.S., and I think we can explore that.

I just would like to piggyback on what Dr. Connolly said around community-based research, and that certainly is something very important for us to be able to do, and we have done a little bit of that.

But those who know, who have done community-based research and have supported it, like the tobacco-related disease research program in California, knows that it takes a lot of time and there aren't a lot of resources to be actually able to do a lot of that work and turn around results that can be presented to committees.

DR. HECK: Would support by the FDA of those community-based organizations in doing the research help you?

MR. LEW: That would be tremendous.

DR. SAMET: Thank you for your

presentation.

Now, we're going to go on to the four three-minute presentations. And remember, you will get a buzzer at three minute and, at that point, please, complete the sentence that you're on.

So we'll begin with Phillip Gardiner from the University of California.

DR. GARDINER: Good morning, and thank you. I have no financial relationships with any of the sponsors.

I guess there's been a lot of discussion this last two days about taste and flavor, and, in my short comments, I want to focus right in on that, I guess because at bottom, the question here, the taste and the flavor of menthol cigarette is precisely the problem.

It's a candy flavoring and I would encourage the Tobacco Products Scientific Advisory Committee to make the same recommendation to the Food and Drug Administration that in the banning of the 13 other candy flavorings, that we take the

same logic.

There are not full teams of scientists sent around to look into do vanilla cigarettes lead to greater lung cancer rates versus other types of cigarettes. There were no teams assigned looking into cinnamon and licorice.

It was an a priori decision that candy flavoring would make it easier for people to start smoking. I think that logic needs to be applied to menthol cigarettes directly.

Let's be frank. Menthol is the classic reinforcer. If you're trying to get nicotine into your system and you also have a minty taste going on, you have excitation of taste buds and other sensory phenomena, whatever receptors we target them at. These things, in and of themselves, are triggers for smoking.

So just to put a wrap on it, I do think there needs to be a broader definition of harm. The industry would like us to focus narrowly in on the molecules and the chemistry associated with menthol and while I think that's important, we

know that cigarettes, in and of themselves, kill. So trying to find a death associated greater with menthol may be problematic.

I do think we should look at youth starting smoking in menthol. I'd look at the spurious health messages associated with menthol, look at the inhibition of cessation and the promoting of relapse associated with menthol, and, indeed, the candy flavoring.

At its bottom, menthol is marketed to the most vulnerable sectors of our society. It is indeed a social justice question. All this discussion over the last day that somehow menthol isn't marketed to African-Americans is absurd. The data speaks volumes to it.

Let me just say, in closing, that there are two journals in publication with numerous articles on menthol that will be out before this committee makes its decision. I want to encourage you to be aware of those and to read them over.

At bottom, we all know it, menthol makes the poison go down easier. Thank you very much.

DR. SAMET: Thank you.

Right on time. Any mini-questions for the short presentation?

Patricia?

DR. NEZ HENDERSON: Thank you, Dr. Gardiner. This is a question that I asked yesterday and I asked again this morning about what we are charged with, the impact of the use of menthol in cigarettes on the public health.

In your opinion, Dr. Gardiner, do menthol cigarettes impact the health of African-Americans in a way where it's preventing disease, prolonging life, or promoting health?

DR. GARDINER: Well, African-Americans disproportionately smoke menthol cigarettes and, at the same time, they die disproportionally from lung cancer and a host of other cancers.

I think there's a direct relationship. I do believe that if menthol is taken out of cigarettes, it will lower the smoking rate among African-Americans and, therefore, improve their longevity and add to the public health.

I don't think we need a -- it's not a chemistry question of if menthol is doing it. It's a sensory question. I think the industry was, actually, to our benefit, yesterday focusing us on taste and flavor. If it's the taste and flavor, I don't think the FDA should be in the position of supporting a product that helps the poison go down easier. I would take it out of it. I think it would improve the public health.

DR. SAMET: Jack?

DR. HENNINGFIELD: You mentioned that menthol should be treated as other candy flavorings. And I believe in the FDA rule, I don't remember whether it was 90 or 120 days, but there was a very short, fixed period to ban candy-characterized cigarettes, and I think, I part, the assumption was that that was less than 1 percent of the market, would not cause huge disruption.

Here, if that was done, do you literally mean 90 or 120 days or how would you handle it because of the larger population that would be affected?

DR. GARDINER: I believe it was 90 days. I guess it was October 22nd and the bill was signed on June 22nd. I think this has come up both from previous speakers and in the menthol conference that took places in October of last year about what are some of the unintended consequences.

So what if the FDA did ban menthol cigarettes? I would turn it around to say this; that extraordinary amounts of money need to be focused on the community where cessation services are the worst, and those are in communities of color, in African-American communities, proportionately.

So, yes, I think it would cause disruption, but I think the harm caused by menthol would be greater than the harm that would come from menthol being removed from cigarettes. So, yes, I think we need to be aware of that.

When the gentleman who spoke earlier on the management and the black marketing and things like that, I think that's possible. Let's be

realistic. But I think it would be an important public health step forward.

DR. SAMET: I want to ask you a question around this issue of taste. I think based on our review of the literature from our first meeting and discussions in this meeting, the committee is struggling with this issue of taste. Is there a science of taste or is it simply a matter of preference?

Certainly, chemicals call flavonoids impart taste, and I'm wondering. Is it your position that the flavonoids in menthol are candy-like or are perceived as candy-like and is that the basis of your belief that menthol has this candy character to it?

DR. GARDINER: Well, I base it on the opinion, as an ex-menthol smoker, what attracted me to it was that it tasted better than regular cigarettes. But more broadly and, I guess, more scientifically, I think there are focus group studies done among smokers from the 1960s, from the 1970s, from the '80s, '90s and even into this

decade that show that certain groups, and African-Americans, in particular, think that these products are less harsh.

Some think they're better for you. Not all focus groups show that. But some do think that they're less harsh and like that. So I think flavor plays an inordinate role.

I think it's in the public health's interest to take flavorings, all candy flavorings, not just menthol, not just the 13 that were targeted, but all candy flavorings out of cigarettes.

DR. SAMET: Okay. Susan?

DR. KAROL: Just quickly. You mentioned two articles or two journals. What are the names of the journals?

DR. GARDINER: The first journal will be a special edition in Addiction. It should be out later this year, and I would encourage people to see it. There will be a number of articles on menthol in that.

The second journal will be the Journal of

Nicotine and Tobacco Research for the Society of Nicotine and Tobacco Research. It should be out in January or February of next year, prior to when you guys need to do that.

Many of the people who have spoken at these conferences will be published in those journals. And thank you for asking the question.

DR. SAMET: Dan?

DR. HECK: Just a quick follow-up to a point Jack made. Apparently, the market popularity penetration of these highly flavored, I guess we'll call them novelty products that were banned under the rule, only accounted for about 1 percent or less of the smoking market.

So do you think or is there evidence that that ban did indeed have substantial effect on smoking initiation?

Also, with regard to the concern you expressed about menthol having a disproportionate effect on African-American disease risk, we do have an unusually strong and large database of epidemiology studies, all of which have considered

race in those disease risk evaluations.

I think it's reassuring to note that those are overwhelmingly negative in terms of not finding an elevated disease risk in association with menthol.

DR. GARDINER: Was that a question?

DR. HECK: Yes. I'm sorry. I just wanted to bring some clarity to some of the impressions you've offered. I guess my real question is in regard to your statement about the ban on characterizing flavors, other than menthol being a desirable thing in terms of suppressing youth smoking or smoking in general, is there any scientific evidence, sound science evidence that we can consider here to substantiate the validity of the assertion that the ban on characterizing flavors can have or has had any significant effect on smoking?

DR. GARDINER: First, it's my understanding that it's only been in effect a few months; and, secondly, as you correctly pointed out, they only occupied 1 percent of the market.

In fact, that was the only reason that the compromise, as you know, went down in Congress, that you could get rid of these flavorings because they were episodically, at best, used.

I think when we're dealing with menthol, we're dealing with a whole different thing. It's been used over the course of the last 70 years. It has become a product that is mainly used by certain groups, particularly groups of color, the more vulnerable, women, African-Americans.

I think it is time for the FDA, I particular, now that this is in their ballpark and their jurisdiction, that they take the step forward and actually ban menthol.

I guess the only point I'll make, and I think we should end, flavorings help the poison go down easier. Menthol isn't a poison. It's all those 62 or 64 carcinogens in smoked cigarettes.

If you smoke it and menthol helps you smoke it, then I think we have a public health responsibility to take it out of them.

DR. SAMET: Okay. Thank you. We'll move on to our next presentation, Jeff Stier, American Council on Science and Health.

DR. STIER: Good morning. I'm Jeff Stier, associate director of the American Council on Science and Health. I appreciate the opportunity to give our perspective on the issue in terms of conflicts. We are funded by a very wide range of corporations, foundations and individuals, but we don't list any individual one, but it's very diverse funding.

We are directed by 350 physicians and scientists and led by Dr. Elizabeth Whelan, who, many of you know, has been a leading anti-smoking advocate for more than 30 years.

We'd like to offer a perspective and context. And for the past couple of days, the committee, for many months now, has been looking at menthol and zooming in very particularly on a lot of conflicting data. I don't think there's much conflicting data on the epidemiology, but there's conflicting data -- both sides have been

accused of cherry-picking the data in terms of initiation, cessation, et cetera, and perhaps that's true.

But when you think about it in terms of -- and I recognize the very narrow mission of this group is to evaluate menthol, but just to offer some perspective, given the very conflicting data in the population effects area and initiation and cessation.

You have to ask, with all the conflicting data about menthol, if you asked the same question about anything that a tobacco company does to tobacco to turn it into a cigarette, it seems the best argument, from a population standard, from initiation and cessation, as well, it makes it taste better and people smoke menthol because they taste better; and we want to reduce smoking, so ban menthol.

Well, anything that a tobacco company does to tobacco, that a cigarette company does to tobacco to turn it into a cigarette is being done presumably to make it more appealing.

So I ask you to consider, if you apply this same standard to any part of the process, choosing which leaves they choose, how the leaves are treated, everything that is done is done to make it better. And is the committee prepared to ban, if given the authority, other processes, everything else that is done, or are you just going to require them to sell -- ironically, to sell tobacco leaves, which are the dangerous part of the cigarette when you burn them?

So I think my time is about up. The other point I just want to make in my remaining 45 seconds is that with all this focus on menthol, broadening it out again in terms of the public health goals -- the public health goals, I think, in part, are to help people stop smoking.

The current tools that we have haven't proven to be very effective. Quit rates don't exceed 15 to 20 percent. And I would encourage the FDA, generally, and the committee -- I understand that this is about menthol -- to think for a moment about things like e-cigarettes and

how they might -- with all the limited time you -- with the limited time and resources you have, to consider other things other than menthol, about how we could actually improve public health, like e-cigarettes, harm reduction, smokeless tobacco.

I appreciate your consideration.

DR. SAMET: Thank you for your comments.

Greg?

DR. CONNOLLY: Dr. Stier, you mentioned you take money from a lot of sources. I just want to be specific and try to keep the rules of the FDA.

Does the American Council on Science and Health, have they ever taken or do take money from the United States Tobacco Company, which is now owned by Altria?

DR. STIER: Dr. Connolly, I know that your interest is --

DR. CONNOLLY: No. I'm just asking a question about where you get your money, that's all. I don't need comments about myself. But I'm asking you a question. Have you taken money from

--

DR. SAMET: I will remind you that you don't have to answer the question if you don't want to.

DR. STIER: That's fine. I will repeat what I stated earlier. The American Council on Science and Health, which is led by 350 leading scientists, is supported by no-strings-attached support from a very diverse group of funders, including individuals. We've received support from the Robert Wood Johnson Foundation. Very diverse funding, and we're very proud of that.

DR. CONNOLLY: So you can't answer that question to us.

DR. SAMET: I think he's chosen not to.

DR. STIER: I think I've answered it.

DR. SAMET: Okay. Any other --

DR. STIER: But I appreciate your effort to try to divert the attention from the substantive comments that I've made.

DR. SAMET: Okay. Thank you for your comments.

Other questions from the committee?

[No response.]

DR. SAMET: Okay. Thank you.

DR. STIER: Thank you.

DR. SAMET: Next, Pamela Clark from the University of Maryland.

DR. CLARK: Thank you very much. In 2001 and 2002 -- first of all, I have no conflicts. I'm a poor professor that got myself here.

In 2001 and 2002, we performed standardized observations at nationally representative sample of tobacco retail outlets, 1,543 of them. We counted and characterized all tobacco branded items, such as signs, functional objects, like clocks and built-in and moveable displays.

There is at least one branded object in 97 percent of all stores, and the average number per store was 12 items. The result is that in this country, you can't take a 5-year-old into a store to buy milk without that child being exposed to many intense pro-tobacco messages.

We also collected the price of a pack of Newports and a pack of Marlboros. We found an inverse association between price and the proportion of African-Americans residing in the census tract of the store. The price of a pack of Newports was $0.51 less in tracts with the highest proportion of African-Americans compared to those of the lowest. The difference was $0.39 for Marlboro.

This, to me, tells me there is industry manipulation of price in these stores. Thank you.

DR. SAMET: Thank you.

Questions? Dan?

DR. HECK: Thank you, Dr. Clark. I have one question. It seems to differ with what we had heard on the marketing and advertising. What is the nature of the intense pro-tobacco message that youngsters receive when they go in retail stores?

DR. CLARK: I wish I could have brought some slides to show some of these things. Just the myriad of advertisements and -- it used to be "Alive with Pleasure." Now, it's "Pleasure with

Newport." The signage, the visualization, the power walls, the moveable displays, they're just all over the place and the kids eye view is like this to the counter. So they're seeing all this exactly at their eye view.

DR. SAMET: Jack?

DR. HENNINGFIELD: Dr. Clark, yesterday, we heard quite a bit of discussion and testimony that marketing was not targeted to African-Americans.

What is your reaction to that? I'm trying to understand it.

DR. CLARK: Well, if we had found the same kind of discounting by both Marlboro and Newports, then I would have said there's a possibility it just had to do with what we know to be the direct association between the neighborhood household income and the price of cigarettes.

But because it was different for Marlboro Reds than it was for Newports, I think there's something else going on there. Now, I do have data that I could actually map every single

Newport ad to the neighborhood characteristics. I just don't have the resources to analyze it. It's a massive amount of data.

DR. SAMET: Thank you.

Greg?

DR. CONNOLLY: That was my question.

Did you, in the neighborhood, see a disproportionate level of Newport versus Marlboro advertising?

DR. CLARK: We could only say anecdotally. I mean, sure, you always know when you're in an African-American neighborhood by how many Newport ads there are. But, again, we have the data, it's massive, 1,543 stores is a lot of stores. But it would be quite definitive if we had the resources to analyze it, because we can connect every store with the neighborhood characteristics.

DR. SAMET: Okay. Thank you.

Next, Carol McGruder from the African-American Tobacco Control Leadership Council.

MS. MCGRUDER: Good morning. I'm Carol

McGruder, and I'm the co-chair of the African-American Tobacco Control Leadership Council out of California. And I have basically some observations and questions that I have put together from my two days here.

We've heard the proper and consistent analysis of science, evidence-based conclusions, but I challenge you to think about who the messengers have been these past two days and the historical role of the tobacco industry scientists.

That role is to cast doubt, to prolong and delay actions that would benefit the public, to muddy the scientific landscape. And when they do this, they delay the process of saving live and of doing things for the good of the public.

I would ask, where was the industry scientific community when their CEOs testified before Congress that they believed that nicotine was not addictive? What was their communal response to that in terms of what the science and the data tell us?

I submit that they are, in fact, employees of adjudicated federal racketeers and that the neutrality that they are trying to bring to this process is impossible.

When Dr. Curtin talked about analyzing different government survey data, he did not at all address the flaws in methodology that do not capture African-Americans and caused our rates to be undercounted in all of these surveys.

I applaud Dr. Connolly. We need more community-based participatory research. We are doing some of that research in California, and it's giving us very, very different smoking prevalence rates than what the official rates are, and we are looking forward to publishing that data very soon.

I also would like to talk about yesterday's presentation of Mr. Jones of Lorillard and reporting that African-Americans were not aggressively targeted by Lorillard and the menthol industries.

African-Americans' use of menthol

cigarettes doubled from 1970 until now, it doubled, and that there's a lot more to just the taste of Newports that make African-American smokers smoke menthol cigarettes by over 80 percent in our youth.

I'd also like to just talk about the scientific process for banning the other flavors and that just because it was easier doesn't mean that excluding menthol is not the right thing to do, as well.

Thank you for your time.

DR. SAMET: Thank you.

Questions? Patricia?

DR. NEZ HENDERSON: Thank you for your presentation. I guess, as a member, I'm trying to understand, among African-Americans who are smokers, why there is such a high prevalence of those that smoke mentholated cigarettes, even though the age of initiation is at a later date.

In your view or in your opinion, why do you think that is the case? Because Mr. Jones did say that there was no targeting towards African-

Americans. What is it that is driving this high rate among African-American smokers to choose this form of cigarettes?

MS. MCGRUDER: First of all, I do believe that there was targeting by Lorillard and the other makers of menthol cigarettes that dramatically increased the use of menthol cigarettes by African-Americans.

I also concur with Dr. Gardiner. I briefly smoked menthol cigarettes when I got to college, way from my parents. And so that's a phenomenon in our community that's not really looked at, that some of that later initiation is when youth can get out of the reach their parents.

Luckily, I couldn't take it, so I never became addicted to it. But I did choose menthol because it was easier to get the poison down. I did experiment with other cigarettes. My dad is going to hear this for the first time.

So the menthol was what I settled on, because it was easier to get the poison down and to smoke; anecdotal.

DR. SAMET: Other questions, comments?

[No response.]

DR. SAMET: Okay. Thank you, then.

This concludes the open public hearing portion of the meeting and we will no longer take comments from the audience.

My script says the committee will now turn its attention to address the task at hand, the careful consideration of the data before the committee, as well as the public comments, but actually we're going to take lunch.

I need to read the lunch statement, which you should have in your heads by now. Committee members, please remember that there must be no discussion of the meeting topic during lunch either amongst yourselves, with the press, or with any member of the audience.

So back at 1:00, and thank you to the public.

(Whereupon, at 11:58 a.m., a luncheon recess was taken.)

A F T E R N O O N S E S S I O N

DR. SAMET: We're getting started, without the booming voice, unless needed. I think in terms of the afternoon schedule, I thought we would take about a half-hour for general committee discussion of what we've heard over the last day and a half.

Remember, the discussion should be focused on what we have heard, and this is not future-looking. This is really to reflect on any discussions or clarifications amongst us about what we've heard.

We then need to move to our major sort of agenda item, which is, considering what we heard, to review a list of additional requests to the tobacco companies, and these -- we have compiled a list of what was mentioned during the clarifying questions. It's possible that the list itself needs clarification or that we've missed something.

So we need to do that, and that is our main item for this afternoon. So in terms of

getting out of here and going home, I think there is some incentive to brief and concise discussions, but I think we should have ample time to talk.

There is a list circulating, if you can just indicate where you're going, what airport, and Tom is going to work on transportation.

So let me then just open it up for discussion. We certainly heard a lot of material, and I think the presentations were extremely well prepared and I appreciate how well everything flowed in terms of getting us information within the allocated time.

So let me just, again, open it up for any general discussion, reflections on what we've heard. John?

DR. LAUTERBACH: Dr. Samet, I'd like to make a clarification on a comment that Dr. Connolly made on slide 5 of the Fernandez presentation. If we could get that slide up there -- I don't need Mr. Fernandez, I just need the slide. That's it.

Now, yesterday afternoon, Dr. Connolly commented, if I heard him correctly, that he thought the demise of the Kool share from 1975 to current was a result of the fact that unlike Newport, that the percent menthol or pack menthol, as we call it, in the tobacco increased.

There are actually several other offered explanations, other than the fact that I hired on there in 1980. But I would call a lot of these things that Dr. Connolly could look at are in his paper with Geoff Wayne that came out last summer, called Brand Changes, and, particularly, figure 2 and the references cited therein would go a long way to explaining what happened.

DR. CONNOLLY: John, I blame that on you, because you were with Brian Williamson. I mean, there is no other reason, in my mind -- I'm just saying Kool is 2.5 percent of market, but it's my understanding it's primarily popular with adults who grew older.

So in '75, it was a cohort effect of people smoking high impact menthol. And then

beginning in '75, we're seeing another cohort effect occur with younger people with lower levels of menthol, and that's my only point.

I didn't say they increased or decreased. I'm saying Kool -- and I looked at the Philip Morris documentation just on one year and Kool did seem to have a much higher level than Newport.

I think it would be helpful if the committee got those numbers over the years so we both could take a really hard look at this.

DR. LAUTERBACH: But I think the point I want to make, Dr. Connolly, as indicated in figure 2 of that article you did with Geoff Wayne, there are a number of other alternative explanations that would also be clarified in the references to that article. And we're talking about an article that appeared last summer in Tobacco Control.

DR. CONNOLLY: Thank you, John.

DR. HECK: I think I agree with you, Dr. Connolly. We did hear at least passing mention of the possibility of a cohort effect driving these sorts of analyses, I think maybe

from Dr. Benowitz at the first meeting. And that's always been my impression, as well, looking at these. Kool was relatively more popular in an earlier day and the Kool franchise, I guess, has tended to age with that product and that decline seems to mirror that.

DR. CONNOLLY: I would add, when R.J. Reynolds brought out Uptown, which was a cigarette dedicated to African-Americans in Philadelphia, within that, they referenced lowering the menthol content to make it more comparable to Newport and not like Kool, when they did Uptown to capture that younger African-American male market. It wasn't a female skew.

I agree with you. But I think over time, there seems to be a shift with younger cohorts towards lighter levels of menthol. I agree with you.

DR. SAMET: Neal?

DR. BENOWITZ: I'd like to make a comment about the perceived difference in marketing that the industry stated and then some people like Phil

Gardiner talked about. It seems to me it's hard to disentangle.

The industry says that they market to people who buy their products. So if African-Americans buy menthol cigarettes, they market to African-Americans. And Phil Gardiner says that tobacco companies market to African-Americans and, therefore, African-Americans smoke more menthol cigarettes.

It seems to me that those are really quite consistent, and I'm not sure how to resolve that. But it does seem to me that a lot of the menthol market must be sustained by marketing, and marketing is going to keep a status quo.

I'm not sure what kind of response that someone could make to that, but it seems to me that it's the same issue on both sides.

DR. SAMET: Dan?

DR. HECK: I guess the status quo is a relative term, because as Dr. Connolly mentioned and as, indeed, we heard in several presentations in the last day or two, a significant driver of

marketing efforts in this industry is stealing the other guy's business.

It's not surprising to me, if Newport is very popular now, that others are trying to steal that business, and it's the American way. So I think we heard that represented in terms of capturing the competitors marketplace yesterday, and I think that's a very prominent part of maintaining the status quo from a different perspective.

DR. SAMET: John? Greg?

DR. CONNOLLY : I think we're not the Federal Hazardous Substance Agency. So we're not dealing necessarily with the toxins for the product. I think we're the Food and Drug Agency, so we're looking at drug effects of nicotine and maybe products associated with that.

When we look at drugs, I think drugs have multiple effects directly within the CNS, but there's also chemosensory effects, and I think we got into that yesterday and we sort of got to learn that taste maybe wasn't as important, I

think, as we would think, but other chemosensory effects are important.

I think there's a body of literature out there that would talk about chemosensory effects and its effects on the limbic system, stimulation of the thermal receptors to create smoothness that then communicates to the limbic system receptions.

R.J. Reynolds' presentation on, well, it doesn't affect the airways, but people perceive it as affecting the airways. Perceptions are really the driving force, in some respects.

Then we heard other discussion about harshness and irritation and effect of nosio receptions. That's telling the brain, maybe through the limbic system or through whatever systems there may be, maybe we don't have a mechanistic link, but that you're going to be rewarded with a high dose of nicotine if it gives you an impact.

So I guess, just as a general term, yes, marketing is important, but we're here to look at the product primarily. It's like looking at the

Ford car. We're looking at the drug in the product and we're looking at the constituents that apply to the application of the drug.

I think in doing so, I'd suggest if we're just looking at taste, then let's do taste and take out the chemosensory stuff and just all go home. But there was a lot of response against that. So it appears the chemosensory is a critical issue.

I think the committee then has to explore that and why is it critical. What is the chemosensory perception of smoothness versus harshness? Why is that important to different age groups? How does that contribute to initiation?

I think there are two sources of data that one could examine. One is the internal industry documents, and I think, on a process issue, I hope we can submit, post the meeting, a request for certain documents from the industry that relate to chemosensory perception.

I think the second is going beyond the tobacco area. There are people who have spent

their lives studying chemosensory perception. I think at the University of San Diego, there's a whole group looking at that and looking at effects on dopamine and how it queues to certain sections of the brain about reward phenomenon.

I think we have to look at those issues. Those are really hard, hard, tough issues to grapple with scientifically. But if they are contributing to reinforcing use of the drug because of the chemosensory effects, then I think we ought to incorporate that within what we do.

I know that has made no sense to anyone, but that's what I'm sort of taking home from this meeting. I learned a lot from -- I want to thank everyone from the tobacco industry for educating me so much. I really learned a lot about chemosensory perception over the past few days.

DR. HECK: I think in response to Dr. Connolly's comments, and, in fact, agreeing with many of those thoughts you had, I think it's been long appreciated that the sensory aspects of smoking play a big role in smoking behavior.

I think our understanding that that's a reality does outpace our mechanistic understanding of a lot of the elements of that, and particularly those of us who really aren't smokers or have never been smokers, it's difficult to understand sometimes the sensory elements that people like, I guess, Dr. Rose at Duke has published on, including studies looking at literally IV nicotine compared to a denicotinized cigarette, and with the smokers in the clinical situation reporting that the denicotinized cigarette actually provided more satisfaction, as they described it, than did the nicotine itself.

I think the difficulty we have, which Dr. True touched on, certainly, the expert taste panels and things like that resident at the tobacco companies and perhaps elsewhere have the vocabulary to describe some of those elements that are made to the ordinary consumer who doesn't have that vocabulary and might say something like, "This cigarette just tastes better to me." There may be woven in there a lot of sensory aspects of

the sensation of smoke inhalation that -- it may be manifested only really insofar as they can describe it, as "I don't know, I just like this one better than the other one."

So we have a difficulty trying to apply this neurochemical chemosensory standard to some of this, because, again, even as we heard, in the product development efforts at the companies, it's basically a matter of taste preference evaluation.

DR. CONNOLLY: John, just to respond, I agree with you. I think it was good presentation. I think we can benefit from looking at specific research conducted by the industry that was not presented during the past two days. I think of Project Fresh Start on menthol in Asia done by Philip Morris, just a wonderful document. Philip Morris' research in chemical senses research, a series of meetings, with excellent science. I think we could all benefit. I think the FDA staff could benefit. Philip Morris' work on nicotine optimization, rich, rich information, scientific information. R.J. Reynolds' research on nicotine

dosing.

So there's a lot of good research out there. I think they were very rushed and we're asking an awful lot of questions. But now we have the opportunity to kind of fine tune now and explore the richness of the tobacco industry research. Just ask them for specific or ask them for broad-based.

I don't want to be accused of cherry-picking. But there is richness that I think, unfortunately, they didn't have the time to pursue.

DR. SAMET: So, Greg, I think when we come to the discussion of what else might be needed, I think we should turn to this, but remember this needs to be in the context of the menthol report. So we have to have that focus.

Jack?

DR. HENNINGFIELD: A couple of reflections. First, Greg was just talking about the product versus the marketing. I think one of the things that's very evident is product and

marketing go hand in hand; even with the small manufacturers developing a product based on existing products, formulating it that way, to a degree, basing the marketing on it.

I think it is important for FDA to try to understand the curves on that graph. That explosive rise in Newport might have been a great thing for the company, but that's a terrible thing for public health.

If FDA is doing things right, all of those graphs should start going down. That's the realty. Public health won't benefit unless all of those start going down. And it looks like that will have to address product formulation and marketing.

I'd like to point out that this isn't unique to tobacco. Yesterday, SAMHSA had a press conference on prescription drug abuse, especially opioid abuse, which is going up and FDA has learned it's not just the morphine-like chemical. It's the product, how it's marketed licitly and illicitly, perceptions, and you've got to take a

whole range of measures to address these things.

The last thing, when we look at the data, also, with respect to Asian-Americans, Pacific Islanders, it looks like -- I'd like to know more about that, but it looks like the experiment, if you will, is starting to occur in those communities. And that would be sad if we got to the point with those communities.

Now, my last point. In the last menthol meeting, we had presentations by FDA and other staff. My take-home was that the most serious concerns about menthol were its contribution to initiation, to development of dependence, impeding cessation and targeting minorities. Those were the things that, to me, jumped out and that was part of my summary in that meeting.

We've had presentations and submissions by the tobacco industry that have challenged a lot of that, criticized some of it. I think FDA does needed to look at all of the data, get the original data, look at the federal surveys. Myself and others have pointed out some of the

problems with the industry analyses. I think they have to be looked at carefully.

But at this point, it appears to me that the concerns of menthol with respect to initiation, dependence, cessation and targeting are real. They have to be addressed. I don't know what the best actions are, but I don't think inaction is going to be an option.

I don't think, personally, I know what the best answer is, but that's where I am right now.

DR. SAMET: Okay. Thank you. Just one comment. I think we should come back to this, the question of the data at hand and the initiation question and the inherent limitations of these repeated cross-sectional observations versus following cohorts of experimenters to initiators, et cetera, over time.

Unfortunately, unless the data are elsewhere, perhaps, in some individual researcher's study, I'm not sure we, around the initiation question, have heard what might be the

strongest line of evidence, and I think it's something we should come back to that I think others can contribute to. So I'll make sure we spend a few minutes on that today.

Neal?

DR. BENOWITZ: A point I would like to address now is the question about whether menthol affects how people smoke cigarettes. I think the data we've heard at this meeting convinces me that menthol does have a significant effect, and here is the argument.

We know that menthol cigarettes, as they are chosen by the general population, have higher nicotine and tar deliveries. We also know that menthol cigarette smokers smoke fewer cigarettes per day. So those are things I think everyone agrees with.

The total exposure study, which is the largest biomarker study we have, looks, especially in African-Americans, at nicotine equivalence in the urine. And I want to emphasize that measure, because in research of my own and research by

several other investigators, if you look at the best correlates for tar exposure and for smoke exposure, it's not cigarettes per day. That's not a very good measure. But nicotine equivalence is the strongest measure.

So I'm saying that the nicotine equivalents that were reported are the best measure of smoke exposure. So here we have a situation where menthol smokers are smoking a couple cigarettes less per day, but they have exactly the same nicotine equivalent exposure and, therefore, the same cigarette smoke exposure.

There's only one way I can understand that, and that is menthol is somehow allowing people to smoke higher tar cigarettes, which, according the titration hypothesis, you'd expect them to smoke less intensely. But with menthol, they are smoking those cigarettes more intensely than they would normally smoke a high tar cigarette.

Now, that, I think, could be important not so much with exposure to tar, but for

addiction. There is biological plausibility for the idea that the more nicotine you take in per cigarette, the more reinforcement you get. And if someone is taking in more nicotine per cigarette, then they're getting a faster rise of nicotine in their brain and getting more reinforcement.

We think, for example, people who are fast metabolizers of nicotine who appear to be more addicted may be so, in part, because they get a bigger nicotine boost per cigarette.

So to me, it seems clear from the data we've seen so far that menthol does affect how people smoke high tar cigarettes and that there's a good biological plausibility for how this could affect the addictiveness by that mechanism.

DR. SAMET: Dan, do you have a point to this?

DR. HECK: I'll try to be brief. I know we're kind of lagging behind. It's difficult sometimes. With regard to the earlier displayed graph of Newport, I would remind the committee that although Newport is having its day now, as

other brands have in the past, our written submission include a litany of less successful, dozens upon dozens of unsuccessful Lorillard menthol brands that have been discontinued.

So we may get an erroneous impression here looking at one brand in isolation. Believe me, Lorillard has had many unsuccessful attempts at other menthol products.

Catching up with Dr. Benowitz's observation, I know that the Total Exposure study authors can speak to their own study. But I heard a different conclusion offered by the author, attributing clearly, statistically, I thought, the differential in nicotine equivalence running in accord with the pharmacogenetic or ethnic classification of the smokers.

In other words, the black smokers, that's where the statistical significant was driven and not due to the menthol. At least that's what I thought I heard.

DR. SAMET: To respond specifically, I think on our request list is discussions of

obtaining these data so that they could be analyzed. In fact, I think probably many of us have questions about the data that were presented.

Neal?

DR. BENOWITZ: Just a specific response. What you say about genetic differences is quite valid for cotinine, because cotinine metabolism is affected by race.

The beauty of looking at total nicotine equivalence is that you get rid of any genetic differences and pathways, because you're recovering the total dose. So that should not be affected at all by race. And our study certainly suggests that robustness across races is a measure of the smoke exposure.

DR. SAMET: I'm going to move on to Mark.

DR. CLANTON: My sort of request or wish is related to marketing and marketing data. There was a subtle effect, I won't talk about intent, but a subtle effect to try to separate advertising from the issue of price and price discounting, and I don't think I'm too far out by saying that price

discounts are in the normal armamentaria of marketing.

So, in fact, discounts and where they are and what degree a product is discounted is all a part of marketing. What I would love to see is geocoded data by zip codes, looking at discounts for mentholated cigarettes.

It would be fascinating, A, if they're all the same across the board. That would be really interesting. But, in fact, if discounts of mentholated cigarettes, which are supposed to be higher priced, priced at a premium, actually turn out to be deeper in certain areas compared to others, I think that would be enormously telling.

So I realize that's probably competitive data, but we can get the marketing and sales data and we can do it by geocoding, and, in fact, analyze that. So a map of that would be enormously telling as it relates to the true marketing strategy of mentholated cigarettes.

DR. SAMET: You seem to have the attention of Melanie.

DR. WAKEFIELD: I just wanted to follow-up on that, because I was going to make a similar sort of point. It's really important to also look at that data for non-mentholated cigarettes, but also to look at it for brand, and also to look at it for where taxes have gone up, because taxes -- as we heard, the industry basically uses price promotions to cushion the impact of a tax increase.

So that's going to vary depending on where taxes are going up and when. So it's going to be quite a complex dataset. So I think we need to be careful about how we ask for that.

Dr. Clark's presentation today was very pertinent, because it was brand-specific. So that presentation, she did mention about Newport and she did mention about Marlboro, for example, and I think that those data were gathered at a time when it was known which parts of the country were experiencing tax increases.

As I understand, in the United States, tax increases can happen not just at the state

level, but perhaps at the county level almost, as well. There might be variation there, as well. So the geocoding is very important.

DR. CONNOLLY: I'd like to take a step back and stick with the menthol issue, but just talk about process, because I think we are breaking new ground and, in breaking new ground, must be careful in terms of establishing precedent on how we address this issue, as well as other issues.

The areas that I have concerns with are, one, committee communications, what is the best way we get information -- and I understand it's through the public or through the public record. If that's the case, then we should be explicitly clear to all committee members that if there's a mechanism for communication, just being asked to come in a room or being held in another room with the light off is not a fun experience.

The second thing is -- and this maybe deviates a bit, but updating the committee --

DR. SAMET: Can I ask a clarifying

question about what you just said?

DR. CONNOLLY: Well, just, one, could we have guidance on what happens when we send materials down to the FDA? I'm just told the FDA takes it. And I'm not criticizing. I think it has been an extremely well run meeting. We have a very dedicated staff. But do people read the material? Is it going to be looked at? If we put it on the Website, what happens to it?

I just want to feel that if we put a lot of work and effort into it, that it's going somewhere. I'm just thinking about communications.

The second thing is lexicography in presentations. We saw a very diverse set of presentations here. We didn't see standardization of terms, standardization of methods. I'm sure the drug industry comes up here -- the FDA has very well established standards and I think -- and I'm not saying today or at this meeting, but the FDA should be thinking about how do we standardize this process over time so that we're comparing

apples and apples, and the job sitting here become somewhat easier.

Updating the committee on what's occurring more broadly, I know we can't bring agenda items before this committee, but what's happened with the ban of lights? I'd like to know.

I know flavored cigarettes have been banned, but I go to the Philip Morris Website and I still see the term vanilla and licorice on the Website. Maybe it's not characterizing.

The licensing system came up. That's very important. But, John, I'm just raising a process issue right now as a committee member, probably out of turn.

DR. SAMET: I think we've got the general thing. I want to actually -- Christi and I have noted your issues and I think we will come back to it in terms of process.

DR. CONNOLLY: Thank you.

DR. SAMET: But I think Ursula had -- back to the point here.

DR. BAUER: I'm not quite sure what the discussion topic is at the moment.

DR. SAMET: I think if you have something you want to say, say it.

[Laughter.]

DR. BAUER: So I'm trying to figure out how the smoking landscape would be different if menthol hadn't been used in cigarette products and how the smoking landscape would be different in the future if menthol were removed from cigarette products.

I'm interested in Dr. Benowitz's point about smoking full flavored cigarettes and that potentially being an important variable.

So if I understand your line of argument, having menthol in a product like Newport allows people to smoke a full flavored cigarette when maybe they would have chosen a light cigarette had menthol not been available.

So the comparison in terms of the data is most people, in fact, do smoke light cigarettes. So when we look at menthol cigarettes, and

Newport's got the lion's share of the market and the full flavored is the lion's share of the Newport market, and we compare that to non-menthol smokers, we're really looking at light smokers on the non-menthol side.

If full flavor is the issue, maybe we need to just be looking at the high tar menthol and non-menthol cigarettes, and that would help us understand what the effect of menthol really is, rather than mix up the range of tar versus one product that's high tar.

DR. BENOWITZ: I'll just make one response. My point was that normally we think if people are smoking high tar cigarettes, that there'd be compensation, say, to smoke less intensely, but we don't see that happening with menthol high tar cigarettes. They're actually taking in more per cigarette than people smoking regular cigarettes.

DR. BAUER: Regular high tar cigarettes.

DR. BENOWITZ: Yes. So I think what you're doing is seeing menthol changing how people

smoke cigarettes and allowing them to smoke higher tar cigarettes.

DR. SAMET: I think just a general comment, too. I think this general idea of -- I'm sorry if I get fancy, but this idea of the counterfactual world in which menthol didn't exist is -- it's a complicated question.

I think the same issue has arisen as at least epidemiologists have thought about how to look at the effects of changing tar yield over time, because essentially no one ever smokes a cigarette that was made in the 1950s forever. The comparator is always, in fact, changing, which I think really makes the job difficult here for sorting out sort of the choices of those who choose to smoke menthol at one time or another are different from those in the past.

I think this is a -- to oversimplify it, this is a very complicated set of problems and I think we have to come down -- drill down to the questions that are informative to our task out of this.

You seem to have gotten the attention of Dan and John, or John or Dan.

DR. HECK: Just a very quick comment on that. We do have countries around the world where menthol is essentially unknown on the market. So it's an imperfect model, I know, but there wasn't time to get into this and it's less relevant to our U.S. situation here.

But frankly, the youth smoking, for instance, in the international dataset, which, admittedly, are more varied in quality and time, I think, looked a lot like the U.S. one. There's really no relationship between the presence of menthol and youth smoking, for instance.

So let's keep ourselves open to the possibility that this information, with all the other that's been reviewed, is informative that menthol really doesn't have a substantial effect on youth smoking or, as we've seen in a number of biomarker studies, does not independently seem to contribute to biomarkers.

I think the studies where tar and

nicotine yields have been matched or are relatively matched in the menthol versus non-menthol comparisons have not seen those differences.

So from many different angles, I think we see a fairly substantial scientific conclusion offered that menthol is really not making a difference in those things.

DR. SAMET: Thank you.

John, do you have a comment?

DR. LAUTERBACH: Particularly, NCI Monograph 13, I basically thought the conclusion there was that pretty much everybody is smoking about the same; whether lights and full flavors, they're all pretty much smoking the same and that's why we can't rely upon the Cambridge filter/FTC method anymore.

DR. SAMET: Okay. Not to re-raise the monograph -- actually, I think I want to move us on, if that's okay. I think the other topic maybe just briefly to come to and then we're going to go -- I'm sorry. I've been told I missed Patricia.

Did you have a new area to cover? We can take a few minutes more and then we're going to go to our list.

DR. NEZ HENDERSON: Sure. Actually, I want to apologize. I apologize on behalf of our ancestors that introduced the sacred tobacco product to the industry. So I apologize.

DR. SAMET: But remember, it was Columbus who, I think, put it in the boat.

DR. NEZ HENDERSON: What I took away from this is that there's -- I agree with a lot of my colleagues where they focus on the science part of it, but there's something happening among African-American communities, as well as Asian communities, where the rates are so much higher compared to the rest of the population.

For us to really understand the impact of why that is happening is really critical. I take the cultural side, because it's very critical for me in the work that I do. So if we can really address that, maybe -- okay. Thank you.

DR. SAMET: Dorothy?

DR. HATSUKAMI: I just want to make a comment that in terms of the information that was presented on cessation, I think that one of the issues that was raised is that the information that we get in the cessation trials is not necessarily generalizable to the population at large in terms of smokers.

I think we still need to take a look at those clinical trials to determine how potentially menthol might be compromising the efficacy of some of the medications that we have.

So I just wanted to make a point that we should not dismiss the results that we observed from the clinical trials that might potentially show that menthol cigarettes may compromise --

DR. SAMET: So when we look at our list of additional materials, we might want to -- I think it's an excellent point. The generalizability issue I understand, but on the other hand, there's certainly an opportunity potentially to learn what you're describing.

So I have, first, Cathy, then Greg, and

Jack. We have three minutes. So we have a new definition of short. Cathy?

DR. BACKINGER: It's a good thing I'm a fast talker. First, just to correct the conclusion of Monograph 13, because it wasn't that so-called "light," I'm using air quotes now light and low tar were smoked the same as full flavor. But the people that smoke light and low tar inhaled more frequently, held in the puff longer, and had a bigger puff volume.

So that's why there was no difference in health effects from those cigarettes. But I wanted jut to put on the table the issue around youth. And I know that the industry did not present youth data, other than what they analyzed, national survey data. But youth just aren't initiating. They're also becoming dependent and they're also trying to quit.

So whatever literature search and other secondary data analysis can be done to look at not just initiation, but is menthol having an effect at all in dependence among youth, and then, also,

quitting among youth, because just like in the adult population, youth want to quit just as much has adults, about 70 percent. And so we need to look at that, as well.

DR. SAMET: Ursula?

DR. BAUER: I just want to follow-up on Patricia's comment. It only matters that one group smokes one brand at a higher rate than another group, if there's something detrimental about that brand. I mean, nobody is here saying, "Oh, my God, white smokers are more likely to smoke regular cigarettes than menthol, and that's a problem.

I'm not sure that we've established that menthol is a problem, and I think that's the main thing this group is charged with.

DR. SAMET: So we will obviously have more discussion on these issues. Greg, the buzzer goes off in 20 seconds.

DR. CONNOLLY: Thanks, John. Just to Dan's point. Menthol, my understanding of the data, it's not terribly popular outside the United

States. Where it is popular, it appears to be certain Asian countries and the popularity seems to have grown recently, particularly within the Japan, among women; where women didn't smoke, now they do smoke.

In Korea, the women's rights stayed flat, menthol didn't come into the market.

A country like Russia, where there's low female smoking rates, there seems to be a high promotion of menthol. And I don't know really what's going to happen with Russian women's female smoking rights. But if you look at the world, the developing world, primarily women don't smoke. And I am concerned that menthol may become a vehicle by which we see an expansion of smoking among women in the developing world.

What this committee does has great implications for global tobacco policy and I think we have to very carefully look at that then. The WHO is going to be looking at this committee, because --

DR. SAMET: Twenty seconds have gone.

DR. CONNOLLY: -- because of its resources. So I just wanted to correct you, Dan, that if you look at the Japan data, it shows exactly the opposite picture.

DR. SAMET: Okay. Jack, you're the last 10 seconds.

DR. HENNINGFIELD: Yesterday, we heard about menthol and ratings of consumer preference and acceptance. When I asked about questionnaires, it appears that rating scales do include things like liking, satisfaction, and preference.

These kinds of measures are routinely used to assess drugs for addiction potential, and FDA and their controlled substance staff know how to interpret such data.

I think it's important that FDA get all of those data --

DR. SAMET: So that actually leads into where we're going; then the process question, Greg, which was your question, I think.

Christi, you're going to respond. You

want me to respond? I'll respond and then she can see if I have it right.

What I think I heard you saying when we were back on your question about this committee's process itself was a statement of issues that might be of interest to TPSAC, either a particular meeting or over time.

The process that we're involved in, of course, is a public process under the Federal Advisory Committee Act. We announce what we are going to be addressing.

Right now, as a committee, of course, we're focused on the menthol report and developing the information base, the evidence base needed to do our job.

I will assume that over time, this committee -- and this committee has presumably decades to come perhaps -- its role on topics will change.

So I think right now, what we need to think about as we set the agendas is what we need to know about for whatever task is in front of us.

Again, that's not to say that we are solely limited necessarily to menthol. I think if there are other things that come up that we need that are relevant to what we're doing, then we will address them, and we will hear from other subcommittees. And FDA brings topics to the committee for discussion.

So that said, what we're going to do now is look at this issue of what else we might need. We just touched on a little bit of this in our discussion.

The list that you're about to see relates then to additional materials, questions to address from the industry. The list that is here is sort of a compilation of the main topics, and then we had some of the specific -- these are the questions. Okay. So these are our general areas that we have just covered. And then within those, we had identified, as we went through, whether the committee had said would be useful to have in addition in addressing our charge for the report.

So what I propose that we do is go

through these now and make certain that these are items that we consider important and relevant to developing our report that, if so, that they are correctly specified in a way that a request could be responded to. And then are there other bits of information that would be useful.

So why don't we just go through them in order? So the first related to the analysis of the TES or other biomarker data using the Canadian intense method addition to the ISO method.

Neal?

DR. BENOWITZ: John, as I understand the TES, this sentence really -- I'm just confusing two different issues, the TES is a human biomarker study. The Canadian intense method is a machine testing issue. So this is really confusing two different --

DR. SAMET: I thought this was asking for the analysis of the TES data in relationship to the yield from the Canadian intense method.

DR. CONNOLLY: The TES reflects normal smoking behavior based on the CRESS smoking

machine. So the Canadian method doesn't relate to TES. But I think whether we did ask for is menthol yield based on the Canadian test method over time. What was given to us was the ISO method. So I think it would be interesting to see, under a more intensive condition, what menthol yield looks like.

Also, the time trends for certain brands, I think that was a request.

DR. SAMET: To clarify, then. So this is the menthol yield by brand and over time by the Canadian intense.

DR. CONNOLLY: And if they have market share, I think that would e an interesting addition, by age. I think the important thing is sub-brands. We saw brand families presented and I think we can't appreciate the richness of the data unless we see it by sub-brand.

DR. BENOWITZ: John, can I also ask, because this came up. It would be nice to see a ranking of the machine-determined yields by popularity of menthol cigarettes, because I raised

the question about that fact average people smoking menthol cigarettes seem to have much higher tar and nicotine yields compared to regular, and someone said, well, it's because it's just a few products. I'd like to see yield by product share, by brand share.

DR. HECK: I think that information certainly could be probably developed from existing data. Quickly, to Dr. Connolly's comment on the Canadian smoking method.

At least in our written submission, there's a little of that data, but I think the companies that aren't active in the Canadian market really probably don't do Canadian intense smoking routinely. But there's not a lot over time, as I think you've expressed interest in, is my guess.

DR. CONNOLLY: Over time. Okay. I appreciate that.

DR. SAMET: And, Neal, you want another bullet here essentially. Is that fair?

DR. BENOWITZ: It could be separate

bullet. DR. SAMET: But you wanted the machine measured tar yield by --

DR. BENOWITZ: By brand, by market share.

DR. SAMET: For menthol and non-menthol?

DR. BENOWITZ: Tar and nicotine.

DR. SAMET: Tar and nicotine.

DR. BENOWITZ: Actually, I'm most interested in menthol, and for menthol cigarettes.

DR. CONNOLLY: This may seem extremely complex, but I think we were struggling with age group and with race/ethnicity yesterday and I think to your point, Neal, when you bring in racial and age groups, that even makes that much more richer, point number two.

DR. SAMET: So you're suggesting Greg, that there might be data that would provide by age -- I don't think so.

DR. CONNOLLY: If there's industry data on sales, 18 through 25, 25 plus, by level, that, to me, is very interesting. Also, we struggle with the issue of race, having them break data out by race and that would be very interesting to me

if it was available.

DR. SAMET: I think you're really asking if there are data on sales of brand or sub-brand by age and --

DR. CONNOLLY: Menthol level, age and race.

DR. SAMET: Menthol, age and race. I don't think we heard of any such data.

DR. CONNOLLY: Well, the SAMHSA data breaks out menthol brands by age and race.

DR. SAMET: So we're going to come to the survey data. So here, we're just talking about the products. So let's leave it that and let's go to the list, and I think there's an item further coming that may -- so, Jack, I think this next one addresses --

DR. NEZ HENDERSON: Could I just go back to the other point? Neal, wouldn't you want to take a look at the menthol levels, too, in the -- you would want to take a look at the tar and nicotine yield, but also the menthol levels.

DR. BENOWITZ: Sure.

DR. NEZ HENDERSON: Because it seems like

that would be informative.

DR. HECK: As long as there's awareness that there is relatively little of that available. There is some.

DR. SAMET: I'm sorry, Dan. Could you?

DR. HECK: The smoke menthol analyses, there is relatively less of that information than there is traditionally tar and nicotine CO analyses.

DR. SAMET: Actually you wanted menthol level in the product and then, actually, nicotine yield.

So then the third bullet? Those of you who are concerned about scales and questionnaires.

DR. HENNINGFIELD: In this one, I think if we could -- because we asked this last time pretty much and didn't get it. So I wanted to just expand the wording a little bit.

Maybe in determining menthol levels and consumer preference, because that was a term that was used quite a bit, but everything that's related and not just panels. I don't want to not

get something because it was done in a survey or a mall intercept study or something.

So any kinds of studies -- so I don't know what the best wording is. But whatever was used to assess consumer preference.

DR. SAMET: I think when we originally discussed this item, it was in relationship to the poker panels, and the members mentioned that they used a number of different scales, and you said that you would like to see those.

So you would like an additional -- so I guess beyond the smoker panels, what are you thinking, for example, the scales that might have been used in the TES?

DR. HENNINGFIELD: Maybe if we just add any smoker panels or surveys used to assess preference, and I would think the word preference should be in there, because the industry used that quite a bit, because it isn't just -- I think if we just asked for menthol levels, it might be too narrow.

DR. SAMET: Melanie?

DR. WAKEFIELD: So as I understand it, there are two different types of panels, one of the expert panels, so-called, and the other consumers, who are not experts, but who are brought in to test their impressions. And I think we want both of those. So they're likely to be different.

Just as part of your request, this is important for looking at the influence of branding on taste at this point, as well. So to look at studies that look at the impact of branding on consumer taste preferences. So sometimes taste preferences are tested with blinded cigarettes, so the smokers don't know which brand they are tasting. It's a blind taste test. And other times, the brand is presented, as well. And I'd like to look at the difference between how smokes rate cigarettes unbranded compared to branded for various menthol brands, in particular; and, also, how that is perceived by African-Americans and other groups.

DR. SAMET: So stop for a moment. So

actually, the request right now that we're dealing with is the one for the actual instruments, and then you're proposing some additional data that might have been gathered with these other instruments.

So I think let's finish off this question of what instruments that are used for copy studies. And I think just to make clear that smoker panels could comprise -- smoker panels, whether they're expert panels or consumer panels.

So I hypertension that terminology should be sufficiently precise. You want to have the opportunity to examine all the scales, questions on the scaling of those that are used.

DR. HENNINGFIELD: Yes. Examine all of the scales that are used, and I think right now it says for use in determining menthol levels. This is a bigger issue, which is do menthol cigarettes -- do certain people like them more than non-menthol. That's part of how you assess abuse liability or addition potential.

So it shouldn't be limited to for use in

determining menthol levels.

DR. SAMET: So I guess a couple of comments, remembering, first, that our focus is on menthol and this came up when we talked about -- we heard about how this testing was done that the information was -- that consumer preference was assessed and that this was a guide to menthol levels.

So I think any request here needs to be kept in that context in terms of our ultimate objective of obtaining this information.

So I think that in determining menthol levels in cigarettes is germane to our report. It could be that other information may also be germane to our report. So how would you like to change this?

DR. HENNINGFIELD: In determining menthol levels and let's say the effects of menthol on product preference. So that may very well include a menthol cigarette compared to a non-menthol cigarette. And if we're trying to figure out if a menthol cigarette is more addictive, that's part

of what you want to know.

DR. SAMET: Okay. Dorothy, are you happy with this?

DR. HATSUKAMI: Well, it's somewhat relevant to this. It would be interesting to know what criteria is used to determine whether a product should be marketed based upon the results from these questionnaires. So the criteria used to determine product --

DR. SAMET: I think there was some discussion on that point. I'm going to come back. I think, Dan, you were --

DR. HECK: Just a comment or observation for our consideration here. I know that the document request that's pending to FDA on all of these broad topics, I would caution the committee that my sense is that document disclosure is going to be vast and to the extent the committee can satisfy its curiosity with a little narrowing of focus here, every brand and sub-brand -- believe me, it's going to be a very large amount of information that's probably not going to be

digestible in the near future.

So to the extent we can, maybe with consultation, try to narrow the focus to get the questions answered without being overly inclusive, I think we'll do a service to the committee's interest.

I think we would also probably like to understand there are going to be some areas where there just isn't satisfactory information or responsive information. What will be the disposition of those questions if there just is no information or no information that addresses the perceived --

DR. SAMET: Thank you. I think Christi, for clarification, has amplified on what this request is about and this would be for future presentation.

Greg?

DR. CONNOLLY: I totally agree with you, Dan. So to provide assistance to the companies, I would recommend listing specific Bates numbers for documents. Now, NCI has funded 10 years of

document research. A lot of that has gone into products, where we can list specific Bates numbers, so we can really focus here. So the industry doesn't waste time, we don't waste time, and then allow the industry to amplify, to add more.

But to Jack's point, test and measures oftentimes are included in large scientific reports. So what you're really looking for are what are the reports, research, test and measures, and then list Bates numbers.

I think the committee members could be happy to provide Bates numbers so that we're not just on a fishing trip here, that we try to provide focus.

DR. SAMET: Greg, just to be clear, go up to the top. This is not about providing documents, because we're going to back to the questions. I just want to remind everybody what we're up to here.

Future presentations.

DR. CONNOLLY: I'm just saying, for

expediency's sake, that industry has -- well, let's not talk to the documents. We could ask for a chemical research report done by Philip Morris in 1990 or we could ask for the Philip Morris report on Fresh Start, so that we don't waste people's time. Dan, I agree with you.

Then if the industry wants to add more to the record, that's fine. I don't like to, as you say, overwhelm the industry.

I really respect their time and energy, and would be more appreciative of focusing --

DR. SAMET: So I think, again, I'm just going to remind you, this is about future presentations that build on what we heard today on these topics. A separate request has been made for documents.

DR. CONNOLLY: I'm just trying to ask specificity, John. We're trying to be specific here so we don't come back and have total areas either ignored or overwhelmed with data, and I think that we have enough expertise and science here to assist the industry in being specific in

terms of what future data they present.

DR. SAMET: So we are going to make requests around specific topics. I think that is quite distinct from saying that we need to see these documents with particular Bates numbers. Document requests have already been made. So what we're really talking about is future presentations at meetings of the TPSAC and hat we need to hear to amplify and build on what we heard over the last day and a half as we think about our report.

I think there are distinct matters, and the documents are being pursued through another route.

DR. CONNOLLY: Maybe my comments are misdirected then. Then I think that the FDA has an obligation to the committee to look at specific documents to assist us in looking at the issue of menthol and responding to Jack Henningfield's questions.

I think what I heard over the past two days was very responsive to certain areas and unresponsive to others. I would hope that that

wouldn't happen next time, but I'm not sure that it would. But I think if we ask FDA to respond to very specific documents that exist that provide the information Jack is looking for, then that could be very helpful in making the committee work efficiently and address the issues that are pertinent.

DR. SAMET: Just to reiterate. Now, what we are focusing on is future presentations to build on what we heard over the last day and a half.

I think we're going to take a brief -- I'm going to make it a 10-minute break, and then we will reconvene. And remember your rules, no discussions.

(Whereupon, a recess was taken.)

DR. SAMET: We are back and in session. According to the agenda, we have one hour before we are done, which I think gives us some incentive to get done. I guess maybe if we're going to stick to that agenda, that time, which we probably should, in the interest of the Beltway on Friday

in the summer -- in fact, this is not a pretty story.

Tom, I think we're going to -- let's pretend we're actually leaving at 3:30 in terms of getting transportation arranged. So some incentive to get this over with.

At Christi's suggesting, we are going to reorganize a little bit, and these are our main topics. You have a list in front of you, which were the items that we had identified for discussion. This is not the edited version, I think, off the screen.

So what we'd like to do is -- remember, these are for additional presentations at future TPSAC meetings that would expand or clarify what we have heard over the last day and a half in relationship to getting our job done with the report.

I think on the issue of documents, if there are specific documents that might be of relevance to this task, we can potentially say that they should be part of the presentation, and

this is a presentation to TPSAC.

Remember that the documents are being obtained through other routes, including the request to the industry and then the review of the legacy documents that is in progress.

So let's start with characterization of menthol in cigarettes. And I think if I understand this, our initial rewriting of the bullet on levels of -- let's see. It was menthol yields by brand, sub-brand over time, by the Canadian ISO method and the tar yields. This could be fit under characterization. So we could move that up.

DR. HECK: Just a brief comment on this particular topic. If the committee 's curiosities can be satisfied with something other than all brands and sub-brands, because we are talking about a vast quantity of information. It certainly is not any time to generate new information.

I did talk with the representative parties at the break and just an idea of the scale

of the existing request, we are talking about millions of pages in the present request.

So there are a lot of requests and a lot of submissions have been made, and I want the committee to consider the utility of more requests on top of the extant requests, because we're quickly going to overwhelm, I think, any staff's ability to generate and process and understand those documents.

DR. SAMET: Thank you. Corinne?

DR. HUSTEN: So I had a similar sort of clarifying kind of thing. So would it potentially be the leading brands as opposed to all brands and sub-brands, or the leading brand or sub-brands, top 10? It's up to you guys, but that might be one way of --

DR. CONNOLLY: Top 10 brand families. Within the families, we see variation in menthol levels, or maybe brand families with greater than 1 percent of market share.

DR. HECK: My sense is we're still talking about millions of responsive individual

documents.

DR. SAMET: Okay. I think, again, on the time scale here, so just for the committee to keep in mind, if we're talking about future meetings with submissions for an upcoming meeting, I think we do need to be sensitive to this point that Dan raised.

Corinne?

DR. HUSTEN: Just, again, to clarify, this is around future industry presentations, which presumably could be summaries as opposed to producing the documents.

DR. HECK: we have not unlimited resources and personnel and time and preparation, as well. So I just do ask the committee understand that there are realities that intrude on the wish list.

DR. CONNOLLY: Yesterday, we saw a presentation on the growth of Marlboro as a brand family, but there was no understanding of what constituted that and we heard different information about Marlboro Milds, with low levels,

and then Marlboro full flavored.

Could it be the top five brand families, Dan? Would that still be an overwhelming task?

DR. HECK: I don't know the specific answer to that question, but certainly I think the level of understanding of what makes a brand successful or unsuccessful -- what was laid out today I think is close to what is known.

If that was thoroughly understood and controlled, there wouldn't be a need for such competition. So there may not be a whole more to the story other than some additional nuances than what has been presented.

DR. SAMET: So in the interest of making this simpler, if it needs to be, we'll say the top five to 10 brands.

DR. BACKINGER: Just a question on clarifying question number 2. Do you all want a timeframe for that? You did it in 1, you said over time, but I don't see that in number 2. Just a question.

DR. SAMET: You mean how many years of

data.

DR. BACKINGER: Right.

DR. SAMET: Neal, do you want to comment on this?

DR. BENOWITZ: I'd be happy with current data or data over the same time period as the Total Exposure study. So the last few years would be fine.

DR. SAMET: The Total Exposure study was 2002 to 2003, if I remember correctly.

DR. BENOWITZ: In the last five years, you're right.

DR. SAMET: Anything else for characterization? So let's go back to the clinical effects next. So clinical effects.

I think here is where the request for the various test skills, et cetera, would fit, and we had been working on a bullet there.

DR. CONNOLLY: I think I'd just say to Jack, test measures are generally included in conferences and research reports. So what are the research tests to measure as used by each company?

Research is an important term, because the test itself is only part of a larger research.

But the second point is we asked for mechanistic links on chemosensory research, and that's what we got. There are no mechanistic links, and that was probably a bad question to ask.

So I think within this is chemosensory research, including chemosensory research and drop the word "mechanistic."

DR. SAMET: I'm not seeing "mechanistic" in what we just moved.

DR. CONNOLLY: Just research, including chemosensory research.

DR. SAMET: Actually, I think you want a separate item then, if I understand your --

DR. CONNOLLY: Clinical effect would be the chemosensory effect of menthol on the different receptors that were described.

DR. SAMET: So I guess the question is are you looking for the findings of the research. This bullet so far has been about the methods of

the research and the scales and instruments used, the instruments and the scaling of the instruments.

DR. CONNOLLY: Probably for utility, the test and measures will be included within research that they conduct. I think if you just ask for test and measures, I'm afraid what the response will be. I'm trying to be a little bit more specific to help Jack collect that data.

DR. SAMET: I just want to go back to where this started. This really originated from specific discussion yesterday about in the smoker panels, what instruments were actually used to collect the data and how were those results scaled.

DR. HENNINGFIELD: And what were the results, of course. What Greg is raising is of interest, but it's broader, and I'm not sure it shouldn't be a separate item.

DR. SAMET: That was my point, actually.

DR. HENNINGFIELD: I want to make sure we don't have the data related to preference,

acceptance, satisfaction, liking, some of the terms we heard yesterday. That's what I want to make sure that we get.

DR. SAMET: So in the interest of time, is the bullet, as it's written now, item 3, what do you want, Jack, Melanie, Dorothy, Greg, any scalologist, what you want for obtaining the data collection approaches, protocols, et cetera? Is that specified in a way that is appropriate?

DR. HATSUKAMI: Yes.

DR. CONNOLLY: Yes.

DR. HENNINGFIELD: Yes.

DR. HATSUKAMI: But I want to add something where it says describe and provide your scales questionnaire. Again, I think it will be important to have their criteria for product preference. So criteria for product preference.

DR. WAKEFIELD: So in other words, although a whole range of things might be measured, some might be more important than others, and what are those?

DR. SAMET: I think that's probably --

Dan?

DR. HECK: I had a separate item. Again, just to assist the process, we heard Dr. True present, at least describing the Lorillard Company's practices in this area, and research in this whole broad area begins and ends with taste panel preference evaluations, period.

The committee should not be disappointed if there's not much in this area, because I think we heard essentially from all three companies, there's just not a lot of use of this sort of receptor mediated chemosensory effect.

Now, if you extend that to include taste preference, simple enough. Those studies are done, as we heard, with different strategies. But there just is not going to be a lot of relevant information, is my sense.

There has been some academic research funded. We heard a little bit of that from Philip Morris. But there is not going to be any information on that.

DR. CONNOLLY: I agree, but it doesn't

hurt to ask.

DR. SAMET: Corinne?

DR. HUSTEN: So is the question what is the taste research including chemosensory?

DR. SAMET: I think we need two bullets, two items. I think we need number 3, where it says "How do you collect the data," one. Two, and I think this goes back to what Dan is telling us, there may not be so much, but essentially how are the data used in determining, in the end, for our purpose, menthol levels, and I think we've been told about taste preference. And I guess we've heard a little bit that there's some art here perhaps that is not captured in numbers and scales.

Still, I think in terms of this criteria for product preference, actually, really, the question is how are these data used really in determining product characteristics, including menthol level. I mean, there's more to it than menthol level alone. I think in relation to menthol, we've heard about flavoring.

DR. HECK: I guess my sense was that that question had been asked and was part of at least some of the written submissions for this meeting. Certainly, the direct question, can a questionnaire be produced? I guess that's clear enough and I should think the answer would be yes.

But beyond that, I just have a sense that there's this sort of information, particularly like the menthol receptor, really characterized in the year 2002, and we've seen menthol cigarettes around for some decades.

So I think there's just not going to be a lot of product design driven by this sort of research, as I think you're talking about.

DR. CONNOLLY: I think, Dan, we asked for what was the mechanistic basis and by doing so, we were asking for almost like what is the mechanistic basis for lung cancer. We don't know. But that's independent of what we know about chemosensory perception and EEG research that one company has conducted, or on nasal-evoked potential research on menthol.

So I agree with you and I think it doesn't hurt to ask.

DR. SAMET: Jack?

DR. HENNINGFIELD: I think this works and if we do not get information that includes seven point scales with different terms that were mentioned yesterday, then we're not getting what we think is there based on the testimony yesterday.

So I think we should be prejudging how much is there. I heard enough yesterday to suggest that there's material there that is more than just we said it based on how we said it.

DR. SAMET: Before we leave clinical effects, Greg, is there a number 5 that you want concerning mechanistic data?

DR. CONNOLLY: You did it well. No. I think it's fine.

DR. SAMET: All right. Then let's keep going. Biomarkers.

DR. BACKINGER: Except does the question about the characteristic of the consumer panels

beyond under the clinical part? It was question 5 right there, who are on the consumer -- so that belongs under--

DR. SAMET: Sure, that should go up, too. Thanks, Cathy.

DR. BACKINGER: And I think you'd want to be maybe a little more specific about what you want. It's probably all the sociodemographics, as well as smoking history, I'm sure, if they have it; how many cigarettes per day, how many pack years, that kind of thing, as well as -- you think of other research. How often are these consumer panels held and what the sample size is, those kinds of -- I don't know.

DR. SAMET: It seems to me that when we were thinking about this, it really had to do with, I think, generalizability from these panels and understanding who they were.

I'm not sure. Obviously, they smoke. But I'm not sure what other details would be useful in terms of our task. Then presumably there are many, many panels. So I'm not sure, as

you posed it, this is an answerable question. It's perhaps only answerable in a very general way.

Dan?

DR. HECK: I think, really, what we heard, it will take a while to digest, because we did see a lot of material. But there are many types of panels. One company will have panels comprising their competition's smokers to see if they can design a product to compete and steal that business from their competition. Other panels comprise smokers of the copy's own brand.

It's fairly mundane. It's not complicated. It's quite straightforward, really. You get adult consumers of the diversity of products and you try to win them to your product or design a product that will appeal to the competitor's franchise.

That's kind of the end of the story on that. It's fairly plain and ordinary consumer research.

DR. SAMET: It seems to me that in terms

of our task, probably the key issue is how these panels might relate to particular groups who smoke menthol cigarettes, and that's what is important, and are there panels that are selected in such a way as to be representative one way or another.

I'm not sure I know how to get at this with any specificity. Jack, if you have a rescue here, do it. But I think that's what we were interested in, in general.

DR. HENNINGFIELD: Just to be clear, item 5 pertains to all of this, because for these preference, taste, so forth, any data related to age, ethnicity, race and so forth, we should be getting that for any human testing. Right? The way five pertains to anything related to humans and testing.

DR. SAMET: Well, it does, but it may be so general as to be unanswerable, I think. I'm not sure who runs the consumer panels. If there are many, many, many panels, which I suspect is the case, then this may not work.

DR. HECK: And I don't have a sense, as I

sit here. I know there's a mechanism for proprietary information to be disclosed, if appropriate, but I don't have a real sense, frankly, as I sit here, how or if any of this strategy for our development may be proprietary. We'd have to find out.

DR. SAMET: Well, let me ask. We're going to go back. Let's leave this for now. We're going to go back through and give some priority to these, and this one, in part, because it can't probably be very specific and maybe not answerable in any case in a usable way, that we may give this lower priority.

Biomarkers, I think we had some specifics. The TES there, I think we have two items. So these were two requests to Altria. And then there was the last -- the RJRT.

DR. CLANTON: On the requests to Altria about carrying out biomarker studies, we might want to add that they collect additional epidemiologic data, like body mass index or weight, because when you look at biomarkers,

particularly C-reactor protein as it relates to risk of heart disease and measure of inflammation, we know that obesity and overweight can contribute to those numbers.

So if they put a pale that was particularly lean together and sort of measured that, that could be a confounding effect. So if we're going to ask for studies, we need to make sure that body mass index is collected as part of that data.

DR. SAMET: So for now, I think this relates back to potential further analyses of the TES data. I would assume that height and weight were measured in that study and such analyses could be carried out.

DR. HECK: I'm quite certain that all these studies have those basic subject characteristics, as well as qualification and disqualification criteria.

I would encourage the committee or the agency to seek the assistance of Altria and the scientists there, because as you can imagine, I

can only imagine the size of the primary datasets here. I know, Neal, you have a concept of this, how vast, how many gigabytes this data must be.

So I think that Altria scientists really could assist greatly in getting to whatever the questions are here.

DR. SAMET: Thank you. If the data are provided, 'm sure there will be questions; there always are.

Other issues under biomarkers? Neal? Dorothy?

DR. HATSUKAMI: It's not biomarkers, but it's probably easy to put on point number 7, if you can just put "and time first cigarette," as well. So carry out biomarker analysis and, also, I wanted to see time to first cigarette for those who have less than 10 cigarettes per --

DR. SAMET: You want by-time to cigarette, first cigarette. Yes. So just by-time. Anything else here, biomarkers?

DR. BENOWITZ: Just to clarify. Dorothy, do you want by-time to first cigarette or do you

want to have time to first cigarette as another thing to analyze?

DR. HATSUKAMI: Another thing to analyze. So carry out biomarker analysis and time to first cigarette for smokers that smoke less than 10 cigarettes per day. Yes. Sorry.

DR. SAMET: Okay. We're leaving biomarkers. Marketing data. Marketeers?

DR. WAKEFIELD: So this speaks to the issue of price promotions, which we were talking about before. What's up there under number 10 is not adequate.

Clearly, what we were saying before is that if price promotions are used in markets where tax increases occur, then it's going to be fairly time sensitive. I suppose we want to look at perhaps the main menthol brands of each company, to look at the price of Newport before a price promotion and after a price promotion in different states and over time, particularly when there's a tax increase.

I don't know how to ask for that.

DR. SAMET: So I just want to put this, again, in the context of our report. The information would be helpful in informing us why people stay with
-- one of the factors that might keep people with a menthol brand.

DR. WAKEFIELD: Well, it might keep them smoking. It might keep them smoking. It might prevent them from quitting. It might make it easier for kids -- well, it does make it easier for kids to take up, if the price is -- if the effects of a tax increase are cushioned.

The fact that African-Americans tend to be more likely to take up price promotions, I think it's really critical here.

So I think to the extent that price promotions are used as a marketing strategy for the menthol brands, they're going to kind of adversely impact African-Americans because of that.

DR. SAMET: And let me ask, is your question whether price promotions are used

differentially by brand and possibly even differently by brand by at least geographic area as a surrogate for population?

DR. WAKEFIELD: Yes. Thank you.

DR. SAMET: It's really quite a detailed request.

DR. WAKEFIELD: It most certainly is. But actually, it is because it's all done by brand. Of course, it's going to be detailed and we were told this morning it's done by where the menthol smokers are, it's done by where the tax increases occur and so forth.

DR. HECK: I do appreciate that the marketing was part of the interest expressed by this committee in this area, but I guess my own personal sense is that this committee has its hands full or more than full with the core scientific issues. That is our charge.

Certainly, as we tread closer to these business and competitive areas, it may be more and more difficult in terms of the time and effort required and the complexities in dealing with

competitive issues, the return on the time and effort on the part of the committee, as well as the companies, might be diminishing as we get farther afield from the core science issues. Just a sense.

DR. WAKEFIELD: I guess my response to that would be that price is such a huge driver of smoking behavior. And clearly, the industry has admitted that they use price promotions to try and cushion the impact of tax increases.

So I would have to say that it's quite important.

DR. SAMET: I think the issue, as I see it, just to go back to what I said, is the question of whether there is marketing that differentially maintains the likelihood of menthol smokers continuing to smoke, and particularly to smoke menthol, which is what they're doing, versus other products.

I think it's an important question. I guess I'm wondering whether data exists with sort of the granularity that you might need to address

that; and, second, whether, in fact, you wouldn't need to really answer the question analytically, some fairly complicated kinds of analysis and whether such is feasible.

I wonder if we can come up with something that is simple enough that's broader descriptive data that might address the question, which I think is what might be helpful.

I think to ask for a broad set of data over time that somehow is related to tax increases, et cetera, the kind of thing that you might want to do from a research perspective, is not a reasonable request on a short timeframe.

So I know the point you would like to explore, and I guess the question is, is there something that might be more feasibly requested.

Jack?

DR. HENNINGFIELD: Well, I think what Melanie is asking for is vital, because whether it's animal studies of drug-taking or human studies of other additive drugs, price and the idea that you manipulate behavior by price, that's

fundamental.

Maybe we have to narrow it a little bit, but basically what we're looking for is, does tax go up in a state where there's a lot of menthol and there's a promotion to drop the price. That's a marketing tool that's being used specifically for that population possibly.

So I'm not sure how to narrow it, but I think that we need this kind of information if we're going to look at things like the rise in those curves and the rise of menthol in lower income populations, which, in the United States, includes African-American populations.

DR. WAKEFIELD: I think we could look at the top menthol brand for each company. I was just saying I think we could look at the top menthol brand for each company. It's no accident that Newport is going up and Marlboro menthol is going up. That seems very important, to me.

DR. SAMET: Okay. We do have this question about differential price promotion, which is part of the story. But you also want to look

at timing of price promotions in relationship to other factors, including tax increases.

Greg?

DR. CONNOLLY: I think, Melanie, what you're looking for is the results, which I think we should look for, but there's also theory, the methods, the results, as with the biomarker study.

So I would think of asking for marketing strategies, reports, as we heard yesterday from RJR, as well as the results.

Also, I saw presented yesterday -- I counted three, perhaps four, either internal marketing reports or maybe a contracted commercial report. As we've asked for the raw data for the TES study, we should be asking for the raw data, with appropriate proprietary protections for the industry, for marketing reports that were submitted to the committee yesterday.

So there are two points, raw data for marketing reports, the same way with TSE, protecting proprietary interests, and then to what are the strategies, what are the theories, the

methods behind the results of why there's lower prices in Pam's study versus other studies.

Am I clear on that? Is that clear?

DR. SAMET: Again, I want to remind everyone of two things. One is that this is a request for future presentations that would relate to a meeting on a relatively short timeframe, which I think logistically limits what can be requested.

Second, this does go back -- really needs to relate to our specific task and recommendation that then the committee will make in its report.

So I think that we need to think about what information we need with highest priority to address issues in our report; and, second, I recognize it's a whole very complicated set of issues that could look at to try and understand the patterns of menthol use as they have evolved in place, in time, in people.

That's clearly very complicated. It's fascinating. There's a lot that we really don't understand. But what we want to draw out from

this is lessons learned that will, again, inform our report.

So I think this comes back to how can we focus down on something requestable and deliverable that would be helpful to us for this report, and I think we're struggling with it and I can understand, because it's a little hard to get into these complexities without moving from one to another to another, because they are all interrelated.

DR. CONNOLLY: John, to your point, I think rather than having to go around and collect hoards of data around prices in specific geographic areas, let's take a few steps back and just ask for what are your existing reports on marketing strategies relative to price to geographic areas and what do you have that you can show us that you've developed.

That's fairly doable. It should exist. They have marketing agencies. The second is there was data submitted on the effect by the companies yesterday, to get that raw data in-house. It

already exists. Give it to the FDA. Provide proprietary protection and see what that data shows.

I'm not sure if do it for drug pre-market approval or drug marketing, if you get marketing data, but that, to me, would be a fairly simple approach rather than to try to collect pricing data from every state in the union over the past 20 years relative to 40 different types of mentholated brands.

DR. SAMET: Dan?

DR. HECK: I just have a brief question related to Dr. Connolly's comment and if it's appropriate to put this to the FDA, fine. If not, just let me know. This request is being made on behalf of the FDA. I'm wondering. Does the FDA have the economic or business or whatever kind of expertise, marketing, to make such a disclosure useful? Is it appropriate for the FDA to comment on their perspective on the utility or degree of interest in this area? If inappropriate, that's fine.

DR. SAMET: Corinne?

DR. HUSTEN: I think the primary challenge is a feasibility challenge, given the short timeframe that the committee has to produce this report. So I think any way that the request can be framed that the industry can provide them -- there's a lot of information the committee requested at the last meeting and now this one, and there's not a lot of time.

DR. SAMET: I think, again, I'm just going to go back to the key issue here, which is what data or presentations could we request that would be informative as to, in a sense, how we arrived at the particular pattern of smoking and utilization of menthol cigarettes and the facts that maintain that, including price promotion, et cetera.

I'm not sure asking such a simple and naïve question as what determines the place and timing of price promotions, and I think that's sort of the issue. And we think that elevations in price related to tax increases is one of those

factors, and perhaps if we can just simply ask the question and then we'll see what the answer is.

Melanie, would that work?

DR. WAKEFIELD: Well, that's what we were actually told today. We were already presented with that information that, in general, price promotions are determined on the basis of tax increases and where the menthol smokers are and so forth.

DR. SAMET: We have asked if they are differential by brand. I'm going to start by type, so that is one of our --

DR. WAKEFIELD: And we also saw some sort of aggregate data to show that menthol price promotions don't seem to vary compared to non-menthol price promotions, and the argument mustered that, well, that can't be accounted for the change in the share of menthol in the market.

But my point is that when you kind of aggregate it all together, it's not going to show -- when you put all the menthol brands together and just call them menthol, it just obscures all

the brand-specific data, which is so relevant.

DR. SAMET: So how about our number 10 as it's written now? Beyond the, I would say, almost a naïve question, the way I proposed it, which we actually know the answer to in a general way. Would data on number 10 be both providable and useful to us?

DR. CONNOLLY: John, let me just say, I agree with you, I think our job is menthol and I think price is definitely related to it. But to collect all of this data and take away from the issue directly before there committee could be overwhelming.

I think we heard fairly convincing evidence yesterday. I would just ask that -- yesterday, we didn't get the backup information that that presentation was based on. I would just like to see the backup information and take a look at that. I'm sure there's a marketing report by which they established those standards and just to read that.

Melanie, I'm sorry, but I sort of have to

side with John on this one, that this is kind of overwhelming.

DR. SAMET: Christi has suggested that background documents could be provided and they would not be made generally available. They would be redacted and not discussed and they be available to TPSAC.

So if we can maybe put a placeholder here for this and we'll rephrase it. And I do think this is probably -- these general issues will probably become very important as the work of the center moves forward and models are developed for what drives things at a population level. These are the kids of inputs that will be important. Presumably the data will be collected in some detail so that model parameters can be estimated.

DR. WAKEFIELD: John, just under marketing, can I add another question there, which is for the companies to present some information on the effects of packaging on consumer perceptions in the menthol area.

DR. SAMET: Okay. Dan, you're sort of

almost ready to say something.

DR. HECK: Well, frankly, I'm a biomedical scientist and most of us here are physicians, epidemiologists I that field. I don't know if there are any economists or business people among us. I don't count myself in those ranks.

Frankly, about all I know about this area is what I've heard in the last two days of presentations. But I just have this sense that we did hear already outlined that there are various kinds of price promotions, for instance, some maintaining brand loyalty, as well as a new brand that may be on the ascent in the marketplace, trying to get a toehold, I wouldn't doubt, aggressively promoted in various fashions at the expense of a major popular brand that's on the market now.

So I just have this sense that this kind of -- I appreciate there is some relevance to our question here, but this fishing expedition is unlikely, I think, to produce useful information

and really inform our core question here, which regards more our own areas of expertise.

That is, does menthol increase risk? Does menthol, as an independent variable, increase the initiation or inhibit the cessation of smoking? Does it increase biomarker exposure? The more core scientific issues.

That's my own personal perspective here, but certainly the committee is entitled to ask whatever they want.

DR. SAMET: Let me follow-up with Melanie, though. I think the question would be -- in a sense, again, it has to be whether you think that there might be something particular to menthol brands perhaps as opposed to non-menthol brands. I think you're the person with the most expertise in this area.

So is there a way to phrase this that it might be like it's giving more specificity and potentially made more useful, again, to our charge?

DR. WAKEFIELD: Well, marketing is really

part of the product. Marketing is an independent driver of brand choice. And so to the extent that anything related to marketing drives someone to choose a menthol brand, it seems to be pretty relevant, to me.

If somebody can be recruited to a brand fairly young, basically, the company has them for live, because people they don't necessarily switch.

So it seems tom me that there's a huge amount of research that the companies do related to packaging gin terms of consumer perception. So the same cigarette can be perceived to taste very different, depending on what the pack looks like and what the brand name is.

To the extent that apples to menthol cigarettes, I think that's very relevant. I think we need to hear about that.

DR. SAMET: Greg?

DR. CONNOLLY: I would love to see the marketing research behind the change of the name on June 22nd of Salem mild menthol to Salem gold

menthol particularly in light of the recent gold decision.

DR. SAMET: Let's go on to Patricia.

DR. NEZ HENDERSON: Yesterday, in Mr. Jones' presentation, he said there was no targeted marketing towards minorities, race. But I just want to see examples of, I guess, marketing strategies that they use, like among African-Americans, where there -- what were the advertisements like when they were sending them out, because he said it wasn't based on race or ethnicity. Can we get that information from them?

DR. SAMET: Again, it still points back to our task in terms of menthol. I guess both of these -- I think your issue, the packaging issue, really related to whether there's something differential.

I think what we heard is that there is marketing, whether it's direct via the Web, these other methods, to smokers by preference. I recognize there's a circularity in that that becomes problematic.

I guess, again, I would like to have a request that is brief, answerable, and will el pus. So I'm not sure that examples of marketing campaigns is going to move us forward.

DR. NEZ HENDERSON: Well, back in 1970, I think it's at 9872, we wanted to know the rate of smoking among African-Americans for Newport cigarettes. We were looking at that graph. All of a sudden, the graph increases. So we're trying to figure out why, for me anyway, why do African-American smokers smoke more mentholated cigarettes. And we can look at the biological components of it and not really get a better understanding of why this is happening. But if we look at the marketing, there might be something in there that is explaining what is happening, particularly with what the industry is doing to these subpopulations.

DR. SAMET: Neal?

DR. BENOWITZ: I just wanted to get a clarification. If we found that the industry used menthol as a key part of their marketing to sell

to African-Americans, how should we consider that in our decisions about whether menthol should be banned or not? I'm just trying to follow the logic behind this, because what we might find is that, in fact, menthol is a big factor in marketing, because that targets the population.

Is that something we should be considering in terms of then banning menthol, if it's being used for marketing purposes?

DR. SAMET: Well, I think this has to do with the overall public health consequences of menthol, the presence of menthol in cigarettes, which is part of our charge. So I think in that sense, it is applicable.

DR. WAKEFIELD: I mean, that would be exactly the motivation for looking at this.

I guess in terms of packaging, I think we heard from Lorillard that there have been no packaging changes. But for the other companies, particularly Altria, there have been. I think it's quite important in a more regulated market to look at the extent to which packaging changes can

influence consumer choice.

So I think to see some presentation on how changes in packaging or how the results of some of the research that is being done by the companies on the effects of packaging on consumer preferences, particularly for the leading menthol brands, and how those packs have changed over time.

DR. SAMET: We've got something down like that. I think I'm cognizant of time, not much left. I'm thinking that we should go back up and look over our list and see what is there.

I want us to at least put a star on those things that we see most critical, the top two or three. So we're going to go back up to the start. Again, I think in deciding which is most important, I want you to keep in mind our overall charge and timeframe and some sort of the feasibility of providing information.

So characterization. Top three.

DR. BENOWITZ: Are you talking about characterization or are you talking about item 1

or item 2?

DR. SAMET: Item 1, and then item 2. Let's take them separately, although they're quite related, arguably.

DR. BENOWITZ: Item 2, I think we're still trying to struggle about whether menthol somehow changes the characteristics of how people smoke cigarettes, and I think item 2 is certainly relevant to that.

DR. SAMET: Okay. We'll put a little highlight or something on it, a gold star. Remember, we can't put stars on everything. So somebody will have to give up their favorite. We're going to highlight.

So let's go to number -- keep going while they're silent.

DR. CONNOLLY: What I have heard from industry is that the chemosensory effects perhaps makes it easier for initiation, and I know people will criticize that. Therefore, you have an effect on a population and the population seems to be youngsters.

So what I see as priorities, first, making that - examining that chemosensory effect of menthol, whether it be on a thermal smoothing or whether it be a higher effect, and then to try to look at population effect on initiation.

So those are the one-two priorities, in my mind. Marketing, as you said, or price, that does play in, but those are the core issues that I think we, as a committee, have to wrestle with.

DR. SAMET: And I think in terms of the initiation question, in part, some of those answers will have to come from looking at other datasets. And I think that we have this critical gap, unless we can find datasets that are longitudinal, that provide us with how use of menthol versus non-menthol might change over time from first experimentation.

DR. CONNOLLY: Or cross-sectional datasets where there is no history of menthol use. We can argue it statistically, but the industry's knowledge of chemosensory perception may be very beneficial to the committee. And I'm looking at

initiation. I think, again, we're a committee that's charged with looking at drugs and not at -- we're not the Federal Hazardous Substance Agency. So I'm coming back to that.

DR. SAMET: So in dealing with the bullets up there, some of what you're discussing, the point is actually number 4. How are these data used from these -- research that includes the chemosensory research, how is that used to determine menthol levels? I think that captures, I think, what you were saying on the side of research, research findings being used. Not quite articulated the way you said it, but it gets at the core data for making those determinations.

DR. CONNOLLY: We are both trying to assess intent, as well as effect. Industry can have an intent.

DR. SAMET: Right.

DR. CONNOLLY: And then the fourth one would assess effect.

DR. SAMET: So when we go down, this is the clinical effects right now. So remember, we

divided up our requests into the topics, the five areas.

DR. CONNOLLY: Well, John, I'm just saying the term "used," to me, relates to intent. In three, we're looking more at effect. I think you can look at both. You can collapse three and four.

DR. SAMET: We can collapse three and four, if we want. Three was, I think, the methods of this research, and four was how are the outcomes of this research used, which I thought spoke to your point. They are so interrelated that you actually can't ask for one without the other. So let's make them both yellow and move on.

DR. CONNOLLY: I thought Hopkins gave everyone As. That's my understanding.

DR. SAMET: That's Harvard.

[Laughter.]

DR. SAMET: That's two. I think we have one more. That counts as one, in my rules. I think the biomarkers we just have to get more and

whether that's this --

DR. BENOWITZ: Certainly, seven is pretty straightforward to get. So that we should ask for. That will be easy.

DR. SAMET: So let's have seven, and there's a request for the data that, should it arrive, would allow explorations of many.

Anything here, Melanie, that you view as particularly critical? And I guess is nine, for example, particularly critical?

DR. WAKEFIELD: No. I think given the difficulty with number 10, I wouldn't necessarily put that in. I think that's a critical thing, but I think the complexity of it kind of precludes it being a priority. It's so difficult to get at. I'm not confident we'll get what we want.

DR. SAMET: Right, right. I agree. So let's see, we're down to population effects.

DR. BENOWITZ: I think this is really critical to have the published data analyzed by race, stratified by -- not stratified -- separately by race.

So we understand initiation and we understand prevalence, menthol versus non-menthol by race.

DR. SAMET: So I think we are all in agreement about this. I guess the question is, with five minutes left, whether we can do this, are there particularly critical datasets that need to be looked at.

I think in fairness to the industry presentations, we were provided with the three more detailed manuscripts that I think we probably need to go through and see what is in there in terms of the stratified analysis, because we were told that there were much more detailed tables in there, which, remember, there are 36 tables or something.

DR. BENOWITZ: I would ask you, as having much more expertise in statistics than me, if they adjust for something, does that give you the full answer? For me, that's useful to do, but I also like to see separate analyses by risk.

DR. SAMET: Actually, I fully agree. I think the point is that adjusted analyses in the

face of substantial heterogeneity are not necessarily really informative. So I think it's the stratified analysis that we want to be looking and understanding, because otherwise a population diversity that's so important here is, if you will, not available.

I think we should transmit this as a general request, but I think we have to take a detailed look at the papers that we were provided, and, again, there may be other opportunities to make requests for more specific analyses after we've gone through those papers.

But I would not know how to amplify on this in the remaining 180 seconds.

DR. LAUTERBACH: Dr. Samet, is it really your intent that we go over in detail the materials, the written materials that were submitted and then come back for the next meeting with questions or clarifications? How are we going to use those materials going forward?

DR. SAMET: Well, I think they were provided to us as background to amplify on the

presentations. I think we should all become familiar, and I think those people with content area expertise should pay particular attention to the relevant sections.

But I think on this point, with the presentations around the survey data, I think the manuscripts merit detailed attention from those of us who need to plow through them, and I think you know who you are. Have fun.

DR. CONNOLLY: Those datasets are public datasets generated, by and large, by the Federal Government and I think those datasets are available in raw form and staff of FDA should be getting at those datasets and doing in-depth analysis, breaking out, where appropriate, brand information, and we should be looking at that. It's helpful for industry to do this.

DR. SAMET: I think the question here is probably one more of timing than intent, if I understand the situation. Heads are shaking yes. Okay.

Dan?

DR. HECK: If I may, Mr. Chairman, I just want to try to assist us, as a committee, just encourage us to bear in mind Dr. Deyton's and Dr. Husten's charge to this committee, which is to provide a sound science basis for an opinion to guide policy in this particular area.

What is sound science? We need measurable outcomes to support this judgment. We have some very measurable scientific data in hand, biomarkers data, epidemiology; does menthol smoking entail a greater risk.

We have a lot of scientific data in hand already to evaluate adequately. The peripheral questions, speculative, what mechanism might underlie menthol liking or does advertising affect menthol sales disproportionately. Those are only important considerations if there's a net impact on the public health standard that Dr. Deyton has outlined for us.

I just fear that we're getting a little too far afield with the weeds instead of seeing the forest. Is there a public health impact of

menthol in terms of exposure to toxins, chronic disease risk, smoking initiation, or smoking cessation?

I think the best service we can provide to our FDA is to nail down the hard science in those areas, to the extent we can.

DR. CONNOLLY: John, just quickly, the law does not speak to whether menthol is more hazardous than non-menthol. We're not here as the Federal Hazardous Substance Agency. What the law speaks to is population effects. That's initiation and that's cessation, its effect on non-smokers, and I think we should stick to nicotine. We should stick to those additives that affect the delivery of nicotine.

I go back to the last point. If there's existing public datasets on use of the product, I feel much better having staff of the FDA do a thorough analysis of those datasets than have them being analyzed by R.J. Reynolds Tobacco Company, particularly in light of the recent court decision.

DR. SAMET: I think, actually, I'm going to end, because it's 3:30. Jack, sorry. But I think we are going to end with -- I think, David, you're going to make closing remarks.

Just back on the analysis issue, you might speak to future plans for what FDA will be doing. Actually, the question I really want to know is how did somebody ever pick Newport? Why not Boston or Framingham?

[Laughter.]

DR. SAMET: But we can perhaps learn that. David, please.

DR. ASHLEY: First off, I just want simply want to thank everyone for being here, for your input. This has been two very valuable days. I think there's been a lot of discussion on some very complex issues and I really appreciate it, and FDA really appreciates the time and the energy everyone has been putting into this.

Clearly, we are going forward to the process continuing to move forward. We have another meeting that will be scheduled later on in

the year, where we will continue to address these issues and continue to move forward.

We're looking forward to the committee continuing to address this, and then providing the report and giving that to FDA, and we will take that under advisement, along with other aspects that we need to consider in eventually coming forward with something.

More than anything else, I just want to thank everyone for being here, for the effort, for the good discussions, for the scientific presentations, and for the excellent discussion of these very complex issues.

DR. SAMET: Good. I want to thank all the advisory committee members, the panel, for your hard work, the FDA staff for your efforts, and the industry for their presentations.

Thank you, and we will see each other again.

(Whereupon, at 3:32 p.m., the meeting was adjourned.)